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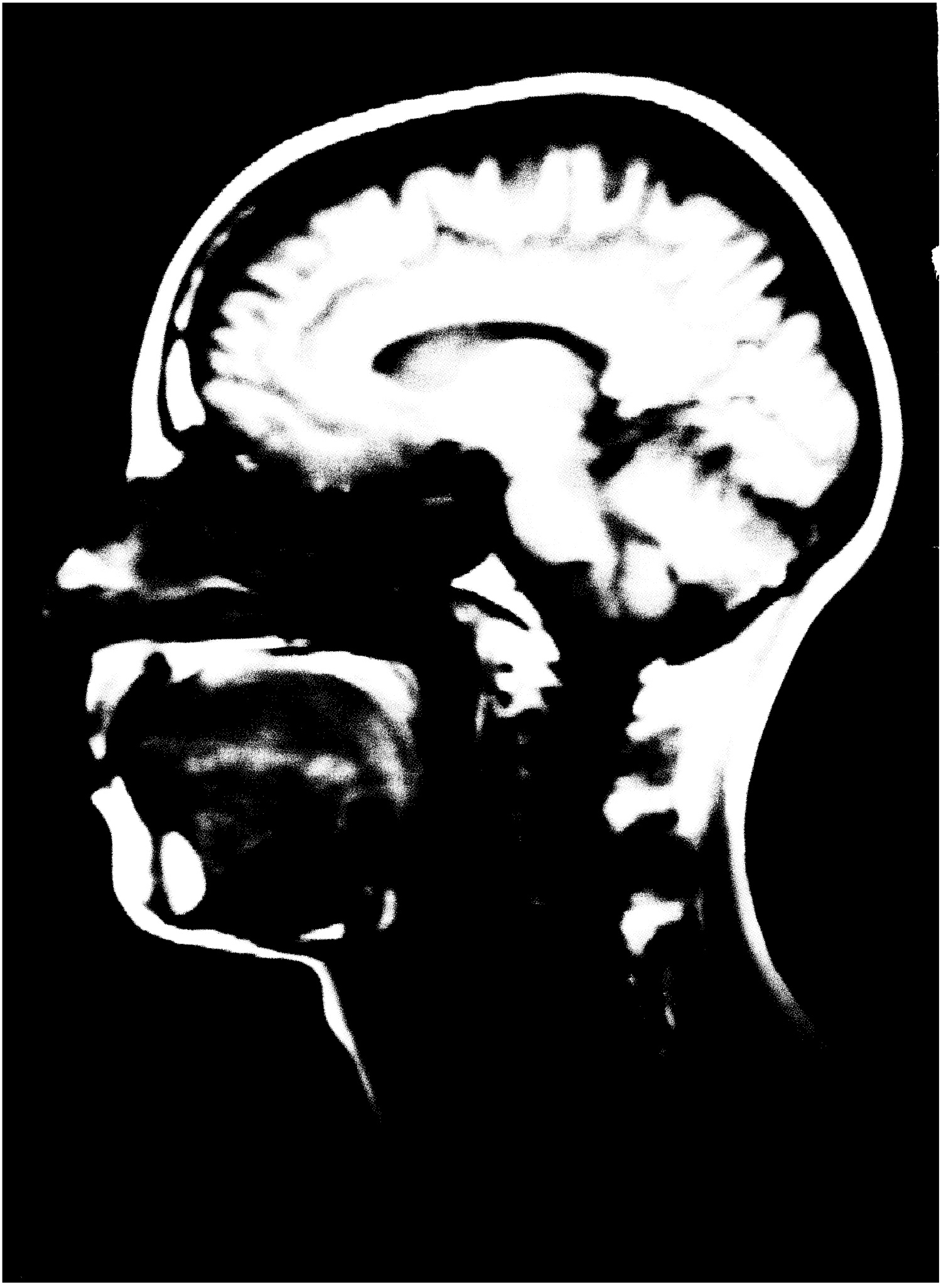

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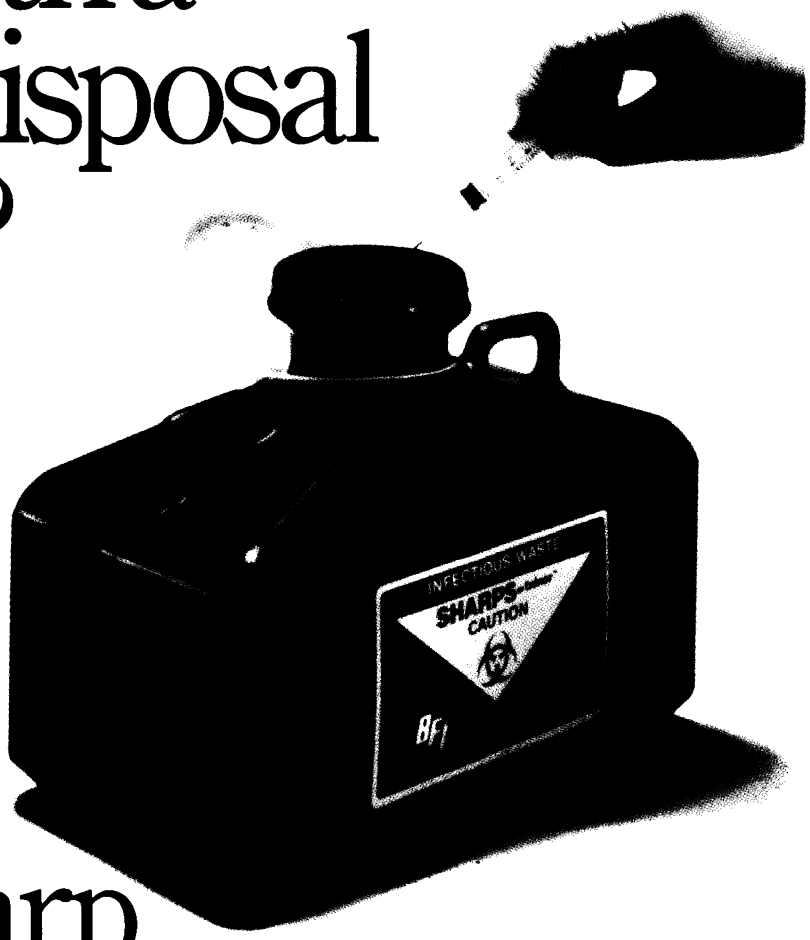

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Calan® SR

Verapamil HCl 180 mg

*The recommended starting dose for Calan SR is 180 mg once daily. Dose titration will be required in some patients to achieve blood pressure control. A lower initial starting dosage of 120 mg/day may be warranted in some patients (eg, the elderly, patients of small stature). Dosages above 240 mg daily should be administered in divided doses. Calan SR should be administered with food.

†Constipation, which is easily managed in most patients, is the most commonly reported side effect of Calan SR.

‡Verapamil should be administered cautiously to patients with impaired renal function.

References: 1. Data on file, Searle. 2. Edmonds D, Würth JP, Baumgart P, et al. Twenty-four-hour monitoring of blood pressure during calcium antagonist therapy. In: Fleckenstein A, Laragh SH, eds. *Hypertension—the Next Decade: Verapamil in Focus*. New York, NY: Churchill Livingstone; 1987:94-100. 3. Midtbø KA. Effects of long-term verapamil therapy on serum lipids and other metabolic parameters. *Am J Cardiol*. 1990;66:13I-15I. 4. Fagher B, Henningsen N, Hulthén L, et al. Antihypertensive and renal effects of enalapril and slow-release verapamil in essential hypertension. *Eur J Clin Pharmacol*. 1990;39(suppl 1):S41-S43. 5. Schmieder RE, Messerli FH, Garavaglia GE, et al. Cardiovascular effects of verapamil in patients with essential hypertension. *Circulation*. 1987;75:1030-1036. 6. Midtbø K, Lauve O, Hals O. No metabolic side effects of long-term treatment with verapamil in hypertension. *Angiology*. 1988;39:1025-1029.

BRIEF SUMMARY

Contraindications: Severe LV dysfunction (see *Warnings*), hypotension (systolic pressure < 90 mm Hg) or cardiogenic shock, sick sinus syndrome (if no pacemaker is present), 2nd- or 3rd-degree AV block (if no pacemaker is present), atrial flutter/fibrillation with an accessory bypass tract (eg, WPW or LGL syndromes), hypersensitivity to verapamil.

Warnings: Verapamil should be avoided in patients with severe LV dysfunction (eg, ejection fraction < 30%) or moderate to severe symptoms of cardiac failure and in patients with any degree of ventricular dysfunction if they are receiving a beta-blocker. Control milder heart failure with optimum digitalization and/or diuretics before Calan SR is used. Verapamil may occasionally produce hypotension. Elevations of liver enzymes have been reported. Several cases have been demonstrated to be produced by verapamil. Periodic monitoring of liver function in patients on verapamil is prudent. Some patients with paroxysmal and/or chronic atrial flutter/fibrillation and an accessory AV pathway (eg, WPW or LGL syndromes) have developed an increased antegrade conduction across the accessory pathway bypassing the AV node, producing a very rapid ventricular response or ventricular fibrillation after receiving I.V. verapamil (or digitalis). Because of this risk, oral verapamil is contraindicated in such patients. AV block may occur (2nd- and 3rd-degree, 0.8%). Development of marked 1st-degree block or progression to 2nd- or 3rd-degree block requires reduction in dosage or, rarely, discontinuation and institution of appropriate therapy. Sinus bradycardia, 2nd-degree AV block, sinus arrest, pulmonary edema and/or severe hypotension were seen in some critically ill patients with hypertrophic cardiomyopathy who were treated with verapamil.

Precautions: Verapamil should be given cautiously to patients with impaired hepatic function (in severe dysfunction use about 30% of the normal dose) or impaired renal function, and patients should be monitored for abnormal prolongation of the PR interval or other signs of overdosage. Verapamil may decrease neuromuscular transmission in patients with Duchenne's muscular dystrophy and may prolong recovery from the neuromuscular blocking agent vecuronium. It may be necessary to decrease verapamil dosage in patients with attenuated neuromuscular transmission. Combined therapy with beta-adrenergic blockers and verapamil may result in additive negative effects on heart rate, atrioventricular conduction and/or cardiac contractility; there have been reports of excessive bradycardia and AV block, including complete heart block. The risks of such combined therapy may outweigh the benefits. The combination should be used only with caution and close monitoring. Decreased metoprolol and propranolol clearance may occur when either drug is administered concomitantly with verapamil. A variable effect has been seen with combined use of atenolol. Chronic verapamil treatment can increase serum digoxin levels by 50% to 75% during the first week of therapy, which can result in digitalis toxicity. In patients with hepatic cirrhosis, verapamil may reduce total body clearance and extrarenal clearance of digitoxin. The digoxin dose should be reduced when verapamil is given, and the patient carefully monitored. Verapamil will usually have an additive effect in patients receiving blood-pressure-lowering agents. Disopyramide should not be given within 48 hours before or 24 hours after verapamil administration. Concomitant use of flecainide and verapamil may have additive effects on myocardial contractility, AV conduction, and repolarization. Combined verapamil and quinidine therapy in patients with hypertrophic cardiomyopathy should be avoided, since significant hypotension may result. Concomitant use of lithium and verapamil may result in an increased sensitivity to lithium (neurotoxicity), with either no change or an increase in serum lithium levels; however, it may also result in a lowering of serum lithium levels. Patients receiving both drugs must be monitored carefully. Verapamil may increase carbamazepine concentrations during combined use. Rifampin may reduce verapamil bioavailability. Phenobarbital may increase verapamil clearance. Verapamil may increase serum levels of cyclosporin. Verapamil may inhibit the clearance and increase the plasma levels of theophylline. Concomitant use of inhalation anesthetics and calcium antagonists needs careful titration to avoid excessive cardiovascular depression. Verapamil may potentiate the activity of neuromuscular blocking agents (curare-like and depolarizing); dosage reduction may be required. There was no evidence of a carcinogenic potential of verapamil administered to rats for 2 years. A study in rats did not suggest a tumorigenic potential, and verapamil was not mutagenic in the Ames test. Pregnancy Category C. There are no adequate and well-controlled studies in pregnant women. This drug should be used during pregnancy, labor, and delivery only if clearly needed. Verapamil is excreted in breast milk; therefore, nursing should be discontinued during verapamil use.

Adverse Reactions: Constipation (7.3%), dizziness (3.3%), nausea (2.7%), hypotension (2.5%), headache (2.2%), edema (1.9%), CHF, pulmonary edema (1.8%), fatigue (1.7%), dyspnea (1.4%), bradycardia: HR < 50/min (1.4%), AV block: total 1°,2°,3° (1.2%), 2° and 3° (0.8%), rash (1.2%), flushing (0.6%), elevated liver enzymes, reversible non-obstructive paralytic ileus. The following reactions, reported in 1.0% or less of patients, occurred under conditions where a causal relationship is uncertain: angina pectoris, atrioventricular dissociation, chest pain, claudication, myocardial infarction, palpitations, purpura (vasculitis), syncope, diarrhea, dry mouth, gastrointestinal distress, gingival hyperplasia, ecchymosis or bruising, cerebrovascular accident, confusion, equilibrium disorders, insomnia, muscle cramps, paresthesia, psychotic symptoms, shakiness, somnolence, arthralgia and rash, exanthema, hair loss, hyperkeratosis, macules, sweating, urticaria, Stevens-Johnson syndrome, erythema multiforme, blurred vision, gynecomastia, galactorrhea/hyperprolactinemia, increased urination, spotty menstruation, impotence.

2/13/92 • P92CA7196V

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PACE PROFILE

Vaughn A. Starnes, M.D. has joined the University of Southern California School of Medicine.

Vaughn A. Starnes, M.D., has joined the University of Southern California School of Medicine as Professor of Surgery, Chief of the Division of Cardiothoracic Surgery and Director of the USC Cardiothoracic Center at USC University Hospital, Childrens Hospital Los Angeles and Los Angeles County+USC Medical Center. Dr. Starnes is a world-recognized leader and innovator in adult and pediatric heart, heart-lung and lung transplantation and treatment of congenital heart disease.

In 1984 Dr. Starnes was accepted to the Stanford Cardiothoracic program, where he completed two years as a resident in cardiovascular surgery, and one year as chief resident in cardiac transplantation under the guidance of Norman Shumway, M.D.

In 1988 Dr. Starnes was appointed director of Stanford's heart-lung transplantation program, and later became chief of pediatric heart surgery and director of the transplant program at Stanford's Lucile Salter Packard Childrens Hospital. He performed about 400 adult and pediatric cardiac cases annually at Stanford. In addition to his adult cardiothoracic surgical expertise, Dr. Starnes earned a national reputation for his work in pediatrics.

Dr. Starnes also pioneered lung and heart-lung transplant procedures in children that previously had only been performed on adults. In 1991 he was the first surgeon to transplant the left upper lobe of a 2-year-old donor into a newborn with pulmonary hypertension who could not be weaned off ECMO (Extracorporeal Membrane Oxygenation). In 1992, he performed the first lung transplant on a baby with congenital diaphragmatic hernia.

University of Southern California

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New Era of Excellence

The arrival of Vaughn A. Starnes, M.D., at the University of Southern California School of Medicine marks a new era of excellence in the treatment of cardiovascular disease. This commitment is exemplified in the creation of the USC Cardiothoracic Center at USC University Hospital, Childrens Hospital Los Angeles and Los Angeles County+USC Medical Center.

Comprehensive Services

The USC Cardiothoracic Center is one of a handful of centers in the country to provide a comprehensive range of adult and pediatric cardiovascular services including adult and pediatric heart, heart-lung and lung transplantation.

The Center features a non-invasive vascular diagnostic laboratory, diagnostic angiography laboratory and state-of-the-art cardiac catheterization laboratories. If indicated, cardiac surgeons incorporate the latest corrective surgical techniques for conditions such as ventricular and atrial arrhythmias and aortic diseases that involve aneurysms and dissections.

The Center also specializes in the treatment of infants with congenital heart defects including hypoplastic left heart syndrome, aortic valve disease, and transposition of the great vessels.

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At the Center, cardiologists, cardiothoracic surgeons, vascular surgeons, radiologists, interventional radiologists and allied medical professionals pool their extensive knowledge and expertise to provide patients with the full range of diagnostic and treatment alternatives.

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As a university-based program, the Center is actively engaged in research. Specialists identify clinical problems and then seek the answer in the laboratory. Patients benefit from this link between bench and bedside, which promises to provide a better understanding of the physiology of the disease process.

Community Resource

As a vital component of the USC School of Medicine, the USC Cardiothoracic Center serves as a key educational resource for community-based and referring physicians. Physicians are encouraged to contact the Center through PACE to obtain telephone consultations, and access information regarding new patient care techniques, medications and research protocols to receive assistance with patient management concerns.

A new era is unfolding at the USC School of Medicine. We invite you to be a part of it. For more information about the USC Cardiothoracic Center, or to refer a patient, dial:
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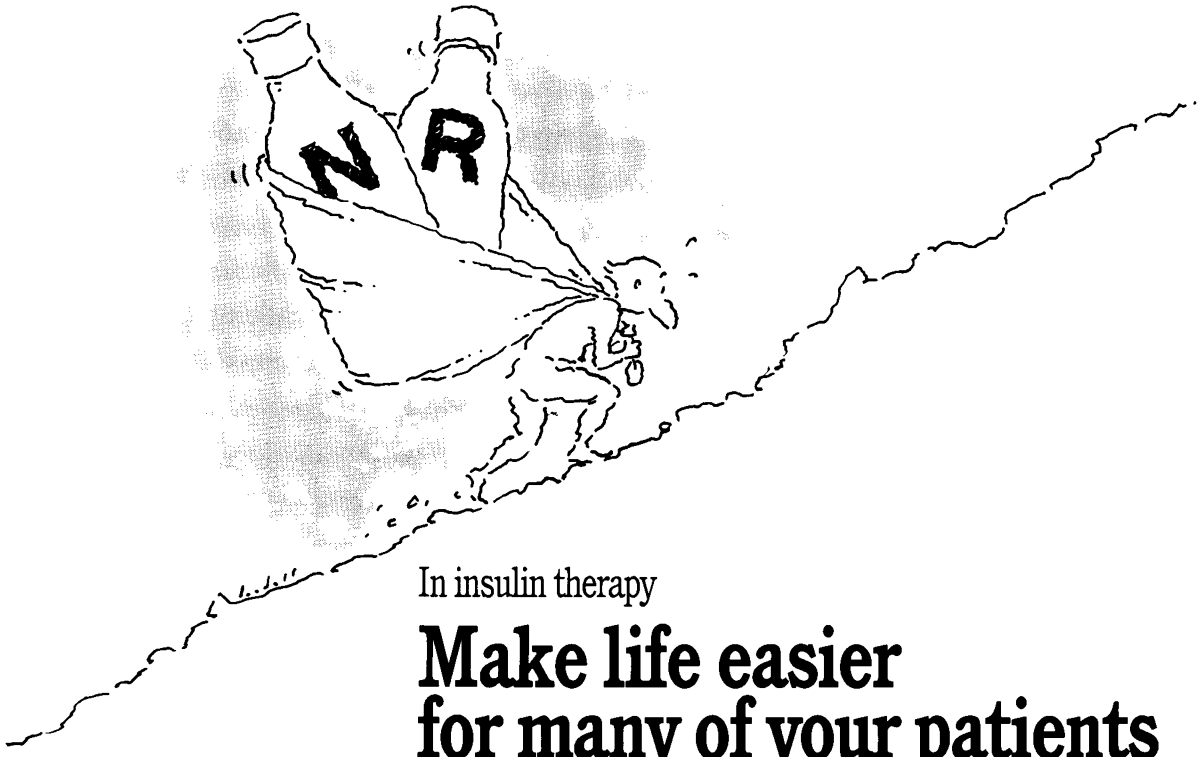

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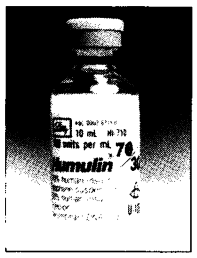

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WARNING: Any change of insulin should be made cautiously and only under medical supervision.

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A favorable side-effect profile[1]

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25% lower cost than Cardizem® SR capsules

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- Start with one 180-mg capsule daily
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*Based on AWP prices.

Cardizem CD is indicated for the treatment of hypertension.

Please see brief summary of prescribing information on next page.

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Switch from Cardizem® SR on a total mg/day basis

For new patients starting on Cardizem® CD:

- Start with one 180-mg capsule daily
- Monitor for 2 weeks
- If necessary, titrate to goal blood pressure

BRIEF SUMMARY

CARDIZEM® CD (diltiazem hydrochloride) Capsules

CARDIZEM® SR (diltiazem hydrochloride) Sustained Release Capsules

CONTRAINDICATIONS

CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, (3) patients with hypotension (less than 90 mm Hg systolic), (4) patients who have demonstrated hypersensitivity to the drug, and (5) patients with acute myocardial infarction and pulmonary congestion documented by X-ray on admission.

WARNINGS

1. Cardiac Conduction. CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (13 of 3,007 patients or 0.43%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.

2. Congestive Heart Failure. Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt). An acute study of oral diltiazem in patients with impaired ventricular function (ejection fraction 24% ± 6%) showed improvement in indices of ventricular function without significant decrease in contractile function (dp/dt). Worsening of congestive heart failure has been reported in patients with preexisting impairment of ventricular function. Experience with the use of CARDIZEM in combination with beta-blockers in patients with impaired ventricular function is limited. Caution should be exercised when using this combination.

3. Hypotension. Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.

4. Acute Hepatic Injury. Mild elevations of transaminases with and without concomitant elevation in alkaline phosphatase and bilirubin have been observed in clinical studies. Such elevations were usually transient and frequently resolved even with continued diltiazem treatment. In rare instances, significant elevations in enzymes such as alkaline phosphatase, LDH, SGOT, SGPT, and other phenomena consistent with acute hepatic injury have been noted. These reactions tended to occur early after therapy initiation (1 to 8 weeks) and have been reversible upon discontinuation of drug therapy. The relationship to CARDIZEM is uncertain in some cases, but probable in some. (See PRECAUTIONS.)

PRECAUTIONS

General. CARDIZEM is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these changes were reversible with continued dosing.

Dermatological events (see ADVERSE REACTIONS section) may be transient and may disappear despite continued use of CARDIZEM. However, skin eruptions progressing to erythema multiforme and/or exfoliative dermatitis have also been infrequently reported. Should a dermatologic reaction persist, the drug should be discontinued.

Drug Interaction. Due to the potential for additive effects, caution and careful titration are warranted in patients receiving CARDIZEM concomitantly with any agents known to affect cardiac contractility and/or conduction. (See WARNINGS.) Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS.)

As with all drugs, care should be exercised when treating patients with multiple medications. CARDIZEM undergoes biotransformation by cytochrome P-450 mixed function oxidase. Coadministration of CARDIZEM with other agents which follow the same route of biotransformation may result in the competitive inhibition of metabolism. Dosages of similarly metabolized drugs such as cyclosporin, particularly those of low therapeutic ratio or in patients with renal and/or hepatic impairment, may require adjustment when starting or stopping concomitantly administered CARDIZEM to maintain optimum therapeutic blood levels.

Beta-blockers: Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers is usually well tolerated, but available data are not sufficient to predict the effects of concomitant treatment in patients with left ventricular dysfunction or cardiac conduction abnormalities.

Administration of CARDIZEM (diltiazem hydrochloride) concomitantly with propranolol in five normal volunteers resulted in increased propranolol levels in all subjects and bioavailability of propranolol was increased approximately 50%. If combination therapy is initiated or withdrawn in conjunction with propranolol, an adjustment in the propranolol dose may be warranted. (See WARNINGS.)

Cimetidine: A study in six healthy volunteers has shown a significant increase in peak diltiazem plasma levels (58%) and area-under-the-curve (53%) after a 1-week course of cimetidine at 1,200 mg per day and diltiazem 60 mg per day. Ranitidine produced smaller, nonsignificant increases. The effect may be mediated by cimetidine's known inhibition of hepatic cytochrome P-450, the enzyme system probably responsible for the first-pass metabolism of diltiazem. Patients currently receiving diltiazem therapy should be carefully monitored for a change in pharmacological effect when initiating and discontinuing therapy with cimetidine. An adjustment in the diltiazem dose may be warranted.

Digitalis: Administration of CARDIZEM with digoxin in 24 healthy male subjects increased plasma digoxin concentrations approximately 20%. Another investigator found no increase in digoxin levels in 12 patients with coronary artery disease. Since there have been conflicting results regarding the effect of digoxin levels, it is recommended that digoxin levels be monitored when initiating, adjusting, and discontinuing CARDIZEM therapy to avoid possible over- or under-digitalization. (See WARNINGS.)

Anesthetics: The depression of cardiac contractility, conductivity, and automaticity as well as the vascular dilation associated with anesthetics may be potentiated by calcium channel blockers. When used concomitantly, anesthetics and calcium blockers should be titrated carefully.

Carcinogenesis, Mutagenesis, Impairment of Fertility. A 24-month study in rats at oral dosage levels of up to 100 mg/kg/day, and a 21-month study in mice at oral dosage levels of up to 30 mg/kg/day showed no evidence of carcinogenicity. There was also no mutagenic response in vitro or in vivo in mammalian cell assays or in vitro in bacteria. No evidence of impaired fertility was observed in a study performed in male and female rats at oral dosages of up to 100 mg/kg/day.

Pregnancy. Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was an increased incidence of stillbirths at doses of 20 times the human dose or greater.

There are no well-controlled studies in pregnant women; therefore, use CARDIZEM in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. Diltiazem is excreted in human milk. One report suggests that concentrations in breast milk may approximate serum levels. If use of CARDIZEM is deemed essential, an alternative method of infant feeding should be instituted.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded from these studies.

The adverse events described below represent events observed in clinical studies of hypertensive patients receiving either CARDIZEM Tablets or CARDIZEM SR Capsules as well as experiences observed in studies of angina and during marketing. The most common events in hypertension studies are shown in a table with rates in placebo patients shown for comparison. Less common events are listed by body system; these include any adverse reactions seen in angina studies that were not observed in hypertension studies. In all hypertensive patients taking CARDIZEM Tablets or CARDIZEM SR Capsules studied (over 900), the most common adverse events were edema (9%), headache (8%), dizziness (6%), asthenia (5%), sinus bradycardia (3%), flushing (3%), and first-degree AV block (3%). Only edema and perhaps bradycardia and dizziness were dose related.

DOUBLE BLIND PLACEBO CONTROLLED HYPERTENSION TRIALS

ADVERSE	DILTIAZEM N=315 # PTS (%)	PLACEBO N=211 # PTS (%)
Headache	38 (19%)	17 (8%)
AV Block First Degree	24 (7.6%)	4 (1.9%)
Dizziness	22 (7%)	6 (2.8%)
Edema	19 (6%)	2 (0.9%)
Bradycardia	19 (6%)	3 (1.4%)
ECG Abnormality	13 (4.1%)	3 (1.4%)
Asthenia	10 (3.2%)	1 (0.5%)
Constipation	5 (1.6%)	2 (0.9%)
Dyspepsia	4 (1.3%)	1 (0.5%)
Nausea	4 (1.3%)	2 (0.9%)
Palpitations	4 (1.3%)	2 (0.9%)
Polyuria	4 (1.3%)	2 (0.9%)
Somnolence	4 (1.3%)	—
Alk Phos Increase	3 (1%)	1 (0.5%)
Hypotension	3 (1%)	1 (0.5%)
Insomnia	3 (1%)	1 (0.5%)
Rash	3 (1%)	1 (0.5%)
AV Block Second Degree	2 (0.6%)	—

The following table presents the most common adverse reactions reported in placebo-controlled trials in patients receiving CARDIZEM CD up to 360 mg with rates in placebo patients shown for comparison.

ADVERSE REACTION	CARDIZEM CD N=324	PLACEBO N=173
HEADACHE	9.0%	8.0%
BRADYCARDIA	4.3%	2.3%
EDEMA	3.7%	2.3%
DIZZINESS	3.1%	3.4%
ECG ABNORMALITY	3.1%	2.9%
AV BLOCK FIRST DEGREE	2.2%	—
ASTHENIA	1.9%	1.7%

In clinical trials of CARDIZEM CD Capsules, CARDIZEM Tablets, and CARDIZEM SR Capsules involving over 3000 patients, the most common events (ie, greater than 1%) were edema (4.9%), headache (4.9%), dizziness (3.5%), asthenia (2.7%), first-degree AV block (2.2%), bradycardia (1.6%), flushing (1.5%), nausea (1.4%), rash (1.3%), and dyspepsia (1.2%).

In addition, the following events were reported infrequently (less than 1%).

Cardiovascular: Angina, arrhythmia, AV block (second- or third-degree), bundle branch block, congestive heart failure, ECG abnormalities, hypotension, palpitations, syncope, tachycardia, ventricular extrasystoles.

Nervous System: Abnormal dreams, amnesia, depression, gait abnormality, hallucinations, insomnia, nervousness, paresthesia, personality change, somnolence, tinnitus, tremor.

Gastrointestinal: Anorexia, constipation, diarrhea, dry mouth, dysgeusia, mild elevations of SGOT, SGPT, LDH, and alkaline phosphatase (see hepatic warnings), thirst, vomiting, weight increase.

Dermatological: Petechiae, photosensitivity, pruritus, urticaria.

Other: Amblyopia, CPK increase, dyspnea, epistaxis, eye irritation, hyperglycemia, hyperuricemia, impotence, muscle cramps, nasal congestion, nocturia, osteoarticular pain, polyuria, sexual difficulties.

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: alopecia, erythema multiforme, exfoliative dermatitis, extrapyramidal symptoms, gingival hyperplasia, hemolytic anemia, increased bleeding time, leukopenia, purpura, retinopathy, and thrombocytopenia. In addition, events such as myocardial infarction have been observed which are not readily distinguishable from the natural history of the disease in these patients. A number of well-documented cases of generalized rash, characterized as leukocytoclastic vasculitis, have been reported. However, a definitive cause and effect relationship between these events and CARDIZEM therapy is yet to be established.

HOW SUPPLIED

CARDIZEM® CD (diltiazem hydrochloride) is available as capsules of 180 mg, 240 mg, and 300 mg in bottles of 30 and 90, and in UDIP® packages of 100.

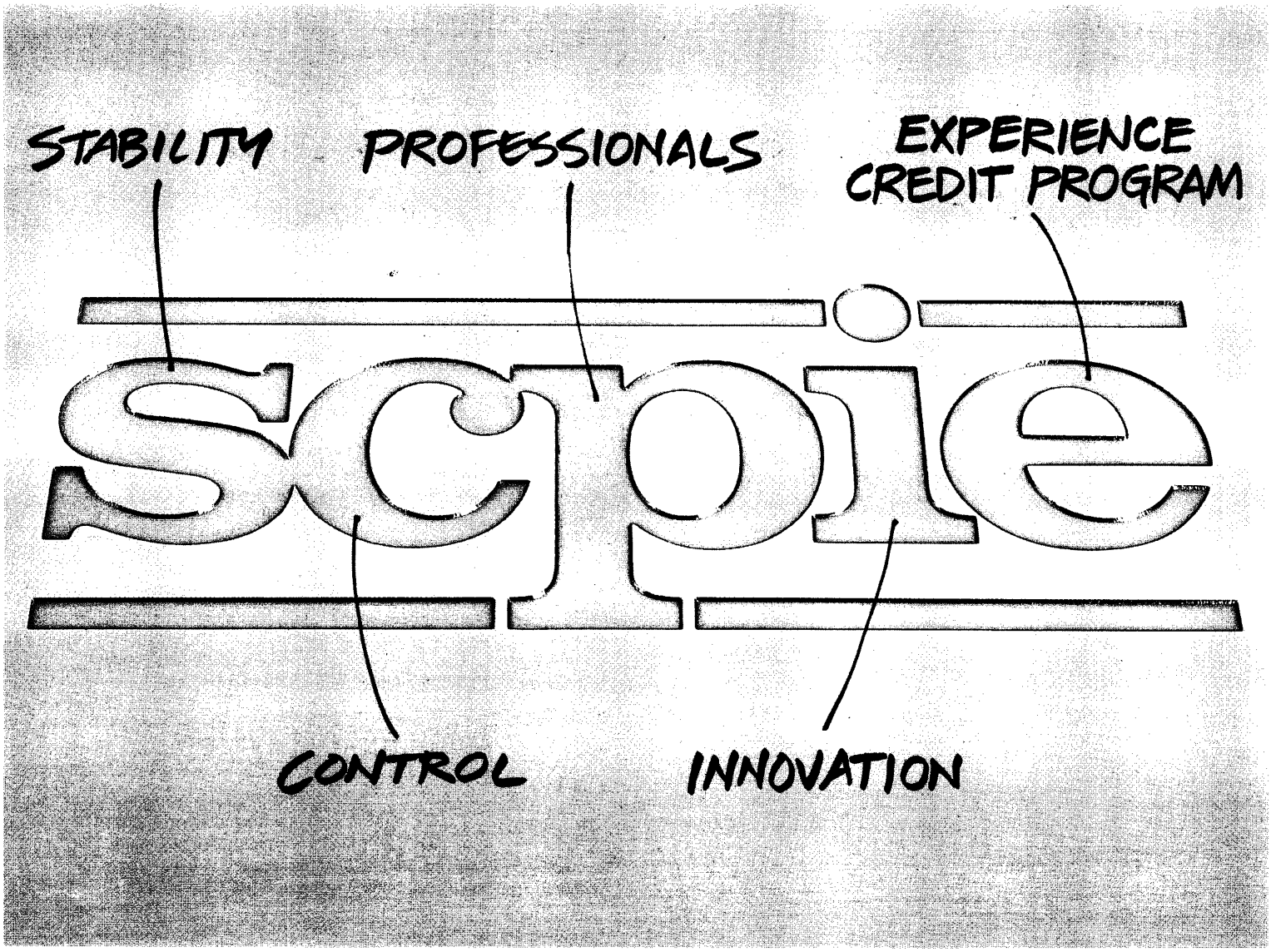
CARDIZEM® SR (diltiazem hydrochloride) is available as sustained release capsules of 60 mg, 90 mg, and 120 mg in bottles of 100, and in UDIP® packages of 100.

CARDIZEM® CD Product Information as of October 1991

CARDIZEM® SR Product Information as of January 1991

References: 1. Data on file, Marion Merrell Dow Inc. 2. Cramer JA, Mattson RH, Prevey ML, et al. *JAMA.* 1989;261(22):3273-3274.

MARION MERRELL DOW INC.
KANSAS CITY, MO 64114



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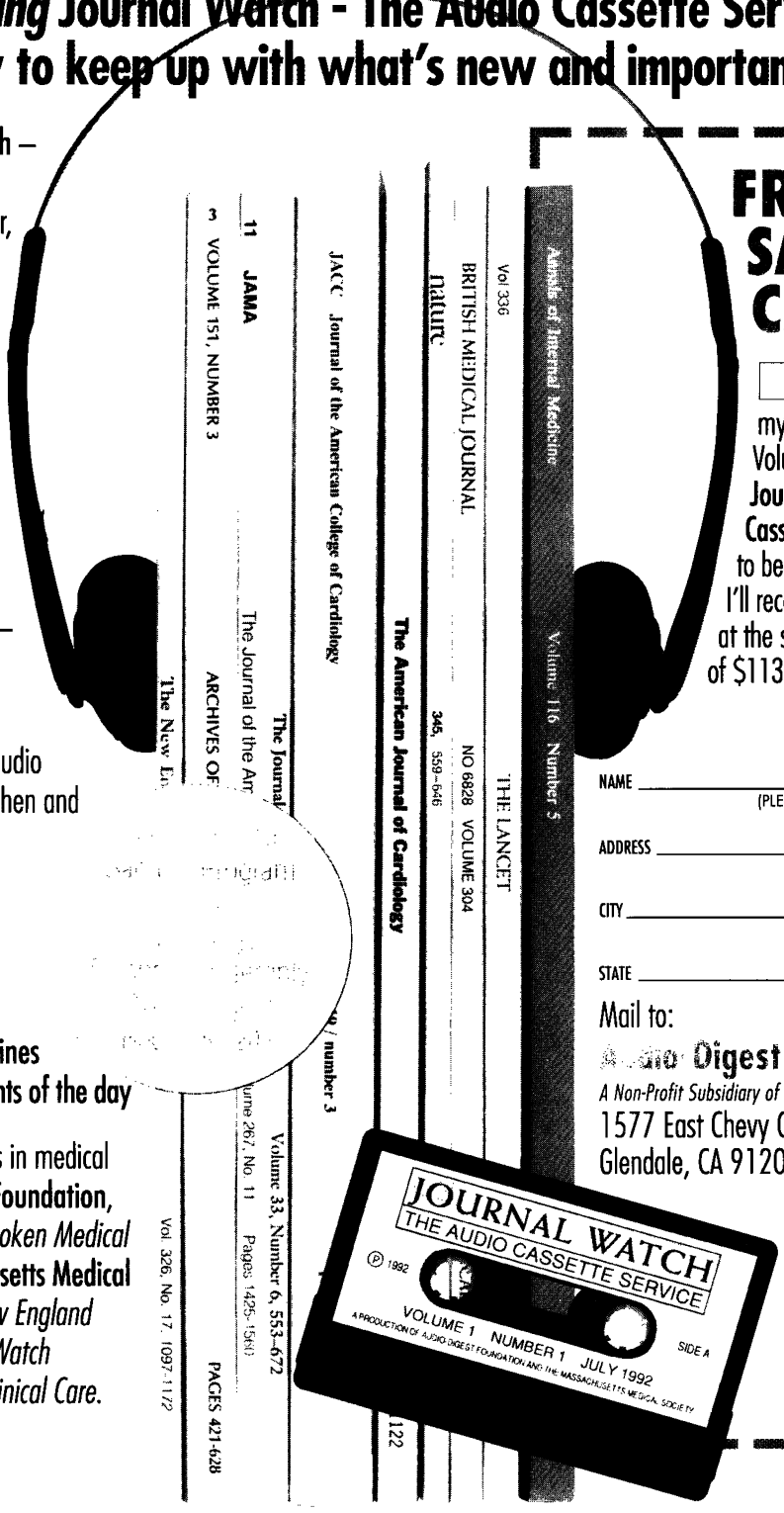

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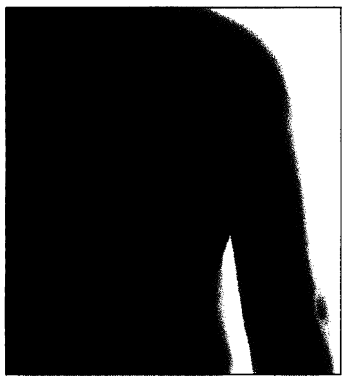
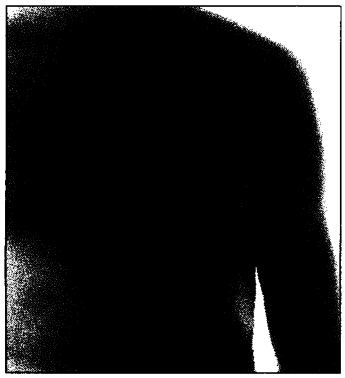
(isradipine)



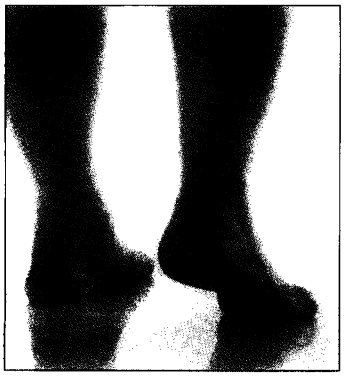
Facilitates renal function.

- No clinically significant change in serum creatinine[1,2] or creatinine clearance[1,3]
- No clinically significant effect on glomerular filtration rate[3-6]
- Maintains or decreases filtration fraction[1,3,6]



Maintains cardiac performance.

- No significant effect on heart rate*[7-10]
- No adverse effect on cardiac conduction[11,12] or contractility†[3,10,13-15]
- No alteration of digoxin clearance[16]

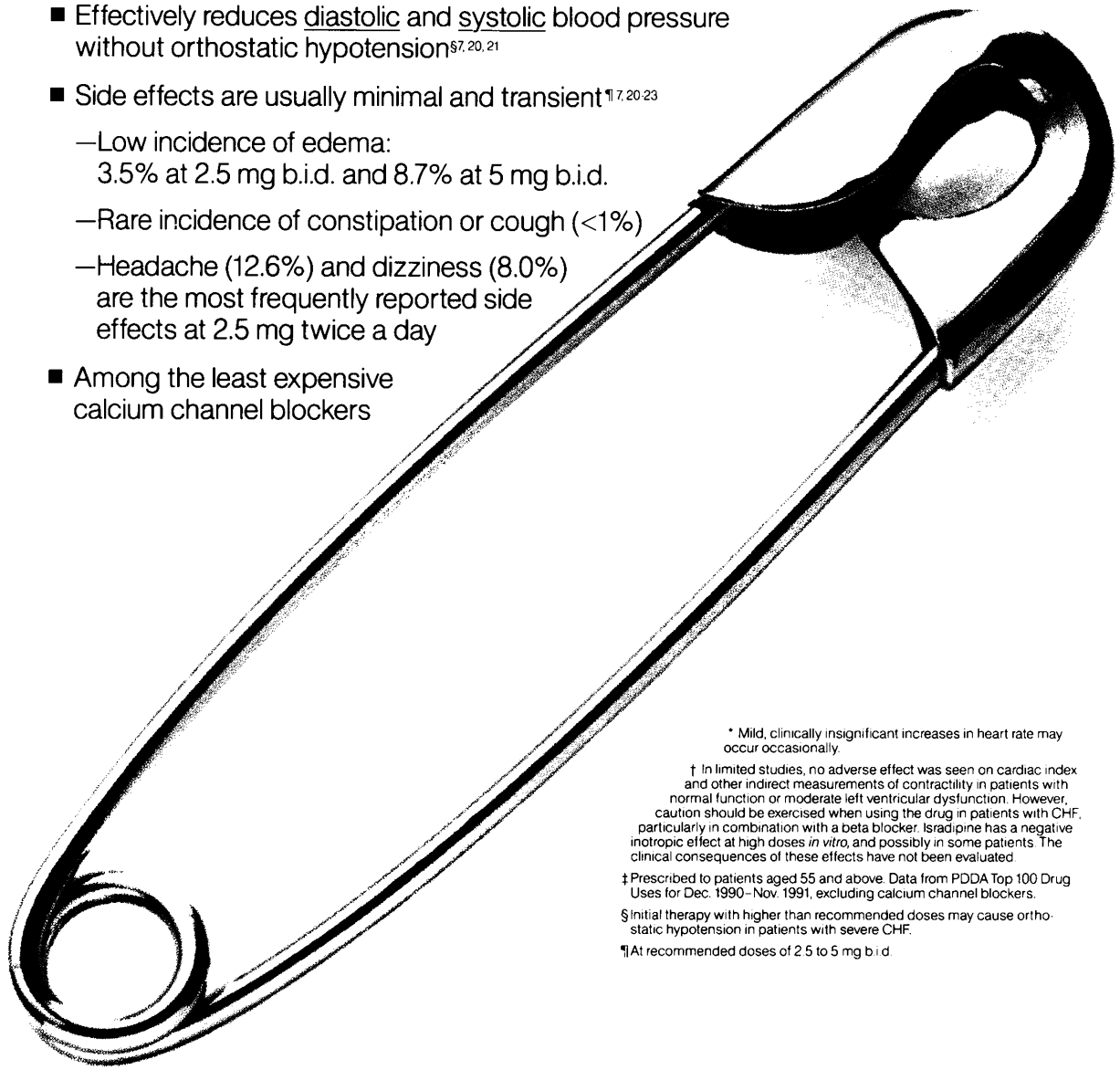


Does not compromise metabolic parameters.

- No clinically significant effect on serum glucose metabolism[17]
- No effect on glucose tolerance, insulin secretion or insulin action in NIDDM patients[17]
- No clinically significant effect on lipid metabolism[18,19]

[redacted]

- No known contraindications except for hypersensitivity to DynaCirc
- No significant interactions with the 20 most-commonly prescribed drugs‡
- Effectively reduces diastolic and systolic blood pressure without orthostatic hypotension§[7, 20, 21]
- Side effects are usually minimal and transient¶[7, 20-23]
  - —Low incidence of edema: 3.5% at 2.5 mg b.i.d. and 8.7% at 5 mg b.i.d.
  - —Rare incidence of constipation or cough (<1%)
  - —Headache (12.6%) and dizziness (8.0%) are the most frequently reported side effects at 2.5 mg twice a day
- Among the least expensive calcium channel blockers



* Mild, clinically insignificant increases in heart rate may occur occasionally.

† In limited studies, no adverse effect was seen on cardiac index and other indirect measurements of contractility in patients with normal function or moderate left ventricular dysfunction. However, caution should be exercised when using the drug in patients with CHF, particularly in combination with a beta blocker. Isradipine has a negative inotropic effect at high doses *in vitro*, and possibly in some patients. The clinical consequences of these effects have not been evaluated.

‡ Prescribed to patients aged 55 and above. Data from PDDA Top 100 Drug Uses for Dec. 1990–Nov. 1991, excluding calcium channel blockers.

§ Initial therapy with higher than recommended doses may cause orthostatic hypotension in patients with severe CHF.

¶ At recommended doses of 2.5 to 5 mg b.i.d.

DynaCirc®

2.5 mg capsules (isradipine) 5 mg capsules

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Please see following page for brief summary of full Prescribing Information.

BRIEF SUMMARY
Please see package insert for full prescribing information.

DYNACIRC® (isradipine) CAPSULES

INDICATION

DynaCirc® (isradipine) is indicated in the management of hypertension. It may be used alone or concurrently with thiazide-type diuretics.

CONTRAINDICATIONS

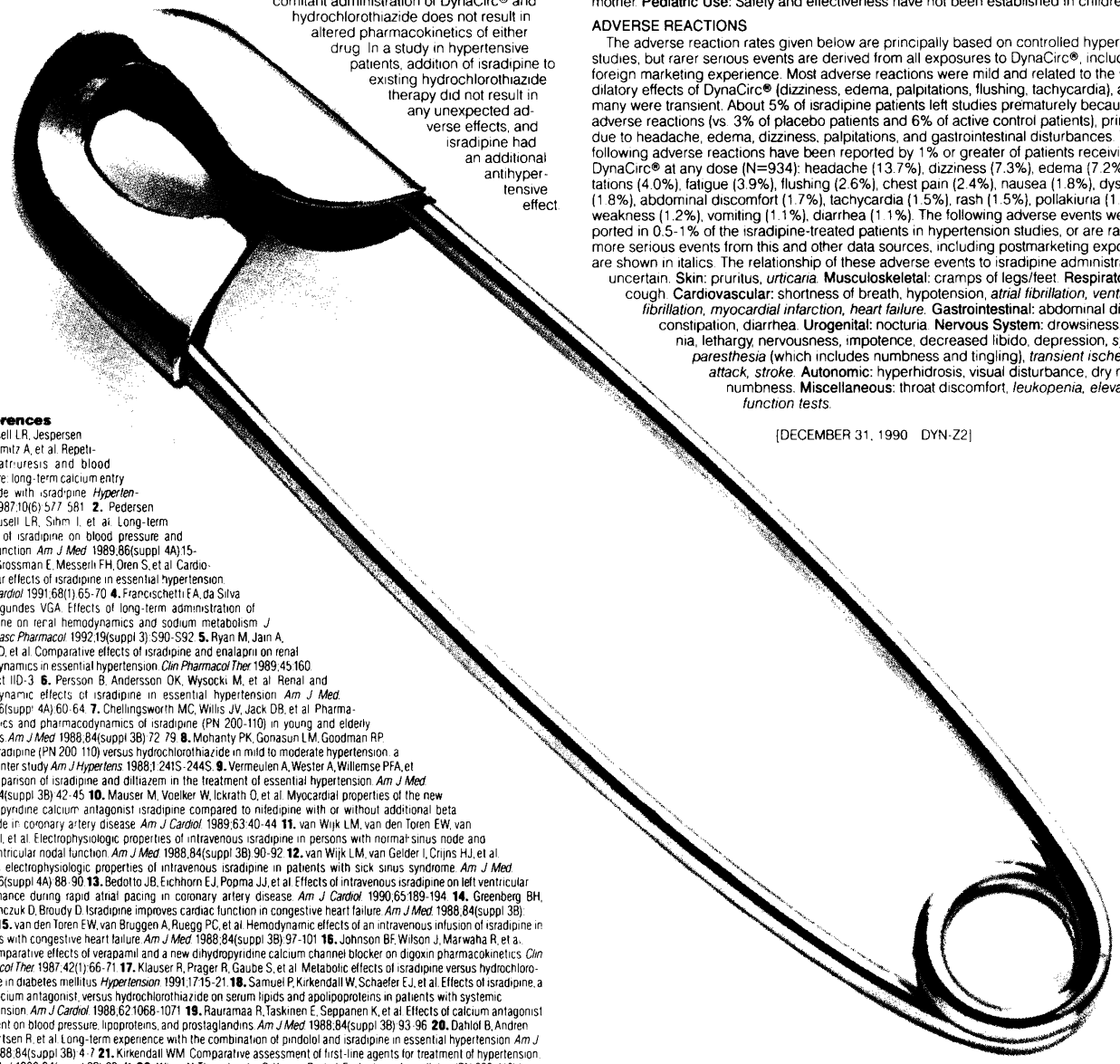
DynaCirc® is contraindicated in individuals who have shown hypersensitivity to any of the ingredients in the formulation.

WARNINGS

None

PRECAUTIONS

General: *Blood Pressure:* Because DynaCirc® decreases peripheral resistance, like other calcium blockers DynaCirc® may occasionally produce symptomatic hypotension. However, symptoms like syncope and severe dizziness have rarely been reported in hypertensive patients administered DynaCirc®, particularly at the initial recommended doses. *Use in Patients with Congestive Heart Failure:* Although acute hemodynamic studies in patients with congestive heart failure have shown that DynaCirc® reduced afterload without impairing myocardial contractility, it has a negative inotropic effect at high doses *in vitro*, and possibly in some patients. Caution should be exercised when using the drug in congestive heart failure patients, particularly in combination with a beta-blocker. **Drug Interactions:** *Nitroglycerin:* DynaCirc® has been safely coadministered with nitroglycerin. *Hydrochlorothiazide:* A study in normal healthy volunteers has shown that concomitant administration of DynaCirc® and hydrochlorothiazide does not result in altered pharmacokinetics of either drug. In a study in hypertensive patients, addition of isradipine to existing hydrochlorothiazide therapy did not result in any unexpected adverse effects, and isradipine had an additional antihypertensive effect.



Propranolol: In a single dose study in normal volunteers coadministration of propranolol had a small effect on the rate but no effect on the extent of isradipine bioavailability. Coadministration of DynaCirc® resulted in significant increases in AUC (27%) and C_{max} (58%) and decreases in t_{max} (23%) of propranolol. *Digoxin:* The concomitant administration of DynaCirc® and digoxin in a single-dose pharmacokinetic study did not affect renal, nonrenal and total body clearance of digoxin. *Fentanyl Anesthesia:* Severe hypotension has been reported during fentanyl anesthesia with concomitant use of a beta blocker and a calcium channel blocker. Even though such interactions have not been seen in clinical studies with DynaCirc®, an increased volume of circulating fluids might be required if such an interaction were to occur. **Carcinogenesis, Mutagenesis, Impairment of Fertility:** Treatment of male rats for 2 years with 2.5, 12.5, or 62.5 mg/kg/day isradipine admixed with the diet resulted in dose dependent increases in the incidence of benign Leydig cell tumors and testicular hyperplasia relative to untreated control animals. A comparable endocrine effect was not evident in male patients receiving therapeutic doses of the drug on a chronic basis. Treatment of mice for two years with 2.5, 15, or 80 mg/kg/day isradipine in the diet showed no evidence of oncogenicity. There was no evidence of mutagenic potential based on the results of a battery of mutagenicity tests. No effect on fertility was observed in male and female rats. **Pregnancy:** *Pregnancy Category C:* There are no adequate and well controlled studies in pregnant women. DynaCirc® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. **Nursing Mothers:** It is not known whether DynaCirc® is excreted in human milk. A decision should be made as to whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother. **Pediatric Use:** Safety and effectiveness have not been established in children.

ADVERSE REACTIONS

The adverse reaction rates given below are principally based on controlled hypertension studies, but rarer serious events are derived from all exposures to DynaCirc®, including foreign marketing experience. Most adverse reactions were mild and related to the vasodilatory effects of DynaCirc® (dizziness, edema, palpitations, flushing, tachycardia), and many were transient. About 5% of isradipine patients left studies prematurely because of adverse reactions (vs. 3% of placebo patients and 6% of active control patients), principally due to headache, edema, dizziness, palpitations, and gastrointestinal disturbances. The following adverse reactions have been reported by 1% or greater of patients receiving DynaCirc® at any dose (N=934): headache (13.7%), dizziness (7.3%), edema (7.2%), palpitations (4.0%), fatigue (3.9%), flushing (2.6%), chest pain (2.4%), nausea (1.8%), dyspnea (1.8%), abdominal discomfort (1.7%), tachycardia (1.5%), rash (1.5%), pollakiuria (1.5%), weakness (1.2%), vomiting (1.1%), diarrhea (1.1%). The following adverse events were reported in 0.5-1% of the isradipine-treated patients in hypertension studies, or are rare, but more serious events from this and other data sources, including postmarketing exposure, are shown in italics. The relationship of these adverse events to isradipine administration is uncertain. **Skin:** pruritus, *urticaria*. **Musculoskeletal:** cramps of legs/feet. **Respiratory:** cough. **Cardiovascular:** shortness of breath, hypotension, *atrial fibrillation, ventricular fibrillation, myocardial infarction, heart failure*. **Gastrointestinal:** abdominal discomfort, constipation, diarrhea. **Urogenital:** nocturia. **Nervous System:** drowsiness, insomnia, lethargy, nervousness, impotence, decreased libido, depression, *syncope, paresthesia* (which includes numbness and tingling), *transient ischemic attack, stroke*. **Autonomic:** hyperhidrosis, visual disturbance, dry mouth, numbness. **Miscellaneous:** throat discomfort, *leukopenia, elevated liver function tests*.

[DECEMBER 31, 1990 DYN-Z2]

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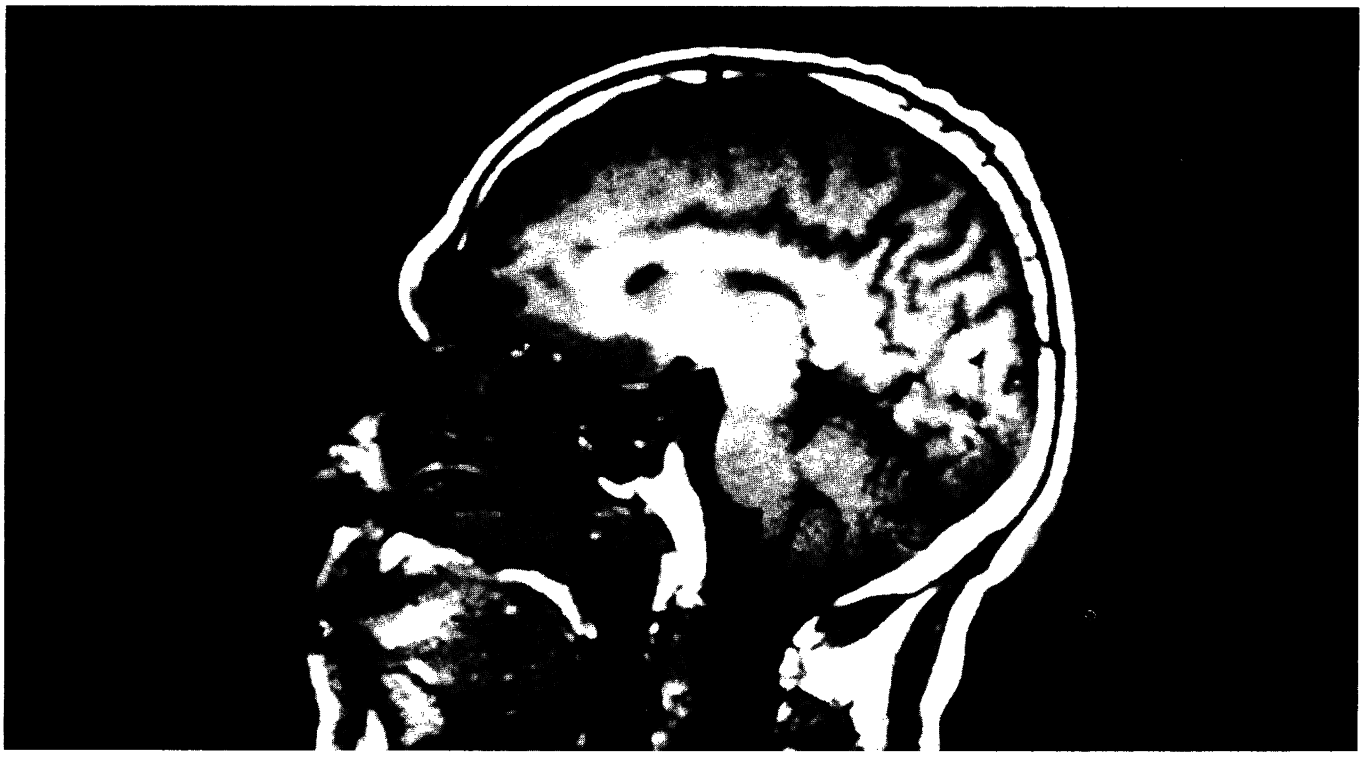

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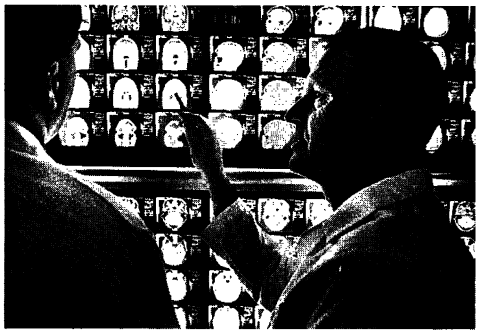

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- public health agencies
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- physicians
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FULL-TIME EMERGENCY PHYSICIANS to join a Level 11 trauma center. Active practice, 39,000 visits annually. Double coverage 24 hours with additional physician coverage during peak hours. Opportunities available for administrative, teaching, and prehospital direction. Located in urban community with significant cultural, recreational, and education resources available. Send CV to Director, PO Box 80412, Phoenix, AZ 85060-0412.

TIME TO CHANGE YOUR LIFESTYLE. Thomas-Davis Medical Centers, an expanding multispecialty group of 180 plus physicians, needs Pediatrics, Internal Medicine, Family Practice, OB/GYN, Urgent Care, General Surgery, Orthopedic Surgery, Urology, Otolaryngology, Ophthalmology, and Retina specialists. Top benefits, profit sharing, guarantee first two years, plus incentive pay, early shareholder. Fee-for-service plus HMO. BE/BC. Call or write Bill De Long; (800) 658-9166, TDMC, PO Box 12650, Tucson, AZ 85732.

CALIFORNIA, PACIFIC NORTHWEST, ARIZONA. Positions in Family Practice, Internal Medicine, Orthopedics, Pediatrics and OB/GYN. Call or send confidential CV to Mitchell & Associates, Inc, PO Box 1804, Scottsdale, AZ 85252; (602) 990-8080.

(Continued on Page 380)

(Continued from Page 378)

PHYSICIANS WANTED

BRING YOUR PARTNER!

A GOLDEN OPPORTUNITY FOR TWO FAMILY PHYSICIANS

PRACTICE TOGETHER in this semi-rural community located 15 miles west of Spokane, Washington.

ADVANTAGES:

- Affiliation and support from a 75 physician multispecialty group.
- Easy access to a regional service and cultural center.
- Established practice with excellent growth potential.
- Up-to-date, modern clinic with a well-trained staff.
- Beautiful recreational area offers year-round opportunities.
- Excellent call schedule and benefit package; salary guarantee leading to early shareholder status.

CONTACT: Colleen Mooney

ROCKWOOD CLINIC, P.S.

400 E. Fifth Ave
Spokane, WA 99202
(509) 838-2531

PHYSICIANS WANTED

SOUTHERN CALIFORNIA

Several positions available to join a multispecialty group, partnership as well as solo practice for the explosive growth of our area population. BC/BE physician in such specialties as:

- FAMILY PRACTICE
- PEDIATRICS
- OB/GYN
- INTERNAL MEDICINE

These excellent practice opportunities offer guaranteed income and a strong referral base.

Strategic location in the Inland Empire minutes from Palm Springs, mountain resorts, Newport Beach, and Los Angeles. University affiliation available.

Contact:

St. Bernardine Medical Center
Janis Pryor, Director Business Development/Provider Relations
or Julie Wagner, Provider Relations Coordinator
2101 N. Waterman Ave
San Bernardino, CA 92404
(714) 883-8711, ext 3063

PUBLIC NOTICE

Department of Corrections
WASCO STATE PRISON
RECEPTION CENTER
701 Scofield Ave, Wasco, CA 93280

The Wasco State Prison Reception Center is accepting applications from Medical Doctors in the fields of General Practice and Internal Medicine to perform medical services to the inmate population on a part-time contractual basis.

Applicants must be fully licensed medical practitioners in the State of California.

Hours of work and compensation will be negotiated at the time of interview. To set up an interview with the Chief Medical Officer, Dr George Girgis, please contact:

Christine McAvoy
(805) 758-8400, ext 5908

Wasco State Prison is located approximately three miles west of the City of Wasco on State Highway 46. The institution houses 4,000 to 4,500 inmates of varying custody levels.

Duties will consist of but not be limited to:

- Diagnostic and general medicine
- Physicals on newly committed inmates
- Emergency medicine
- Daily clinics and sick call

(Continued on Page 381)

(Continued from Page 380)

PHYSICIANS WANTED

PHYSICIAN OPPORTUNITIES NATIONWIDE
For all specialities for hospitals, clinics, multi-specialty groups, partnership and solos. Contact Jim Grant in complete confidence at the bay area specialists. **G & G Physician Services, 1400 Coleman, Ste B-22, Santa Clara, CA 95050; or call (800) 727-2478, FAX (408) 727-7390.** Never a fee to the physician.

ROCKY MOUNTAIN WEST AND SOUTHWEST NEED PHYSICIANS. All specialties needed. Urban, rural, solo, group opportunities, all close to mountain recreation. Call Rita Longino at (800) 279-5267 or FAX CV to (800) 467-1246 or send CV to WHS, PO Box 2107, Corrales, NM 87048-2107.

NORTHERN CALIFORNIA RECREATION AREA. Full-time and part-time salaried position in Ambulatory Care clinic. Enjoy excellent working hours, no night calls, generous benefit package, malpractice insurance provided. Located near the Sierra foothills offering excellent opportunities for hiking, swimming, boating, fishing, and skiing. California license required. Family Practitioner preferred. Call or send résumé to Northern Valley Indian Health, Inc, 2167 Montgomery St, Oroville, CA 95965; (916) 534-8440. EOE Native Americans encouraged to apply. Deadline: open until filled.

INTERNAL MEDICINE BC/BE OPENING due to retirement. Very stable multispecialty group in growing area. Will join department of eight other Internal Medicine physicians. New building on hospital campus. McHenry Medical Group Inc, Attention Thomas Wallace, MD, PO Box 576566, Modesto, CA 95357.

MONTEREY, CALIFORNIA. BC/BE Internist needed to replace retiring partner in busy four member group. Reply to Number 273, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

PHYSICIANS WANTED

NORTHERN CALIFORNIA

SAN JOSE. Leading Primary Care group practice affiliated with 200-bed hospital is growing. BE/BC physicians in the following specialties are needed:

- Family Practice
- Internal Medicine
- Pediatrics
- OB/GYN

A generous salary, good benefits, and a liveable practice schedule are offered. Please send your CV to **Ken Baker, Physician Search Group, 550 Montgomery St, Ste 725, San Francisco, CA 94111;** or call **(800) 229-0411** or **(415) 399-8840; FAX (415) 399-0411.**

INTERNAL MEDICINE—NEVADA, TEXAS, LOUISIANA, FLORIDA! Private practice opportunities available in Las Vegas and Reno, Nevada; Dallas, Victoria, and McAllen, Texas; New Orleans and Shreveport, Louisiana; West Palm Beach, Hollywood, and Plantation, Florida. For details, call Eloise Gusman, (800) 535-7698 or send CV to PO Box 101656, Ft Worth, TX 76185, or FAX (817) 927-0030.

PEDIATRICIANS—NEVADA, CALIFORNIA, TEXAS! Private practice opportunities available. Hospital sponsored with coverage or join an established group. For details, call Eloise Gusman, (800) 535-7698 or send CV to PO Box 101656, Ft Worth, TX 76185, or FAX (817) 927-0030.

FAMILY PRACTICE—CALIFORNIA, NEVADA, LOUISIANA, AND TEXAS! Private practice opportunities available in southern California, Las Vegas and Reno, Nevada, Shreveport and New Orleans, Louisiana with established groups. For details, call Eloise Gusman, (800) 535-7698 or send CV to PO Box 101656, Ft Worth, TX 76185, or FAX (817) 927-0030.

PHYSICIANS WANTED

OB/GYN. Multispecialty group in northwest Washington desires second Obstetrician. Excellent practice opportunity, full range of benefits, early partnership status, all practice costs paid. For more information contact Shane Spray, 1400 E. Kincaid, Mount Vernon, WA 98273; (206) 428-2524.

WASHINGTON. Openings for career oriented Emergency Physicians, BC in Emergency or Primary medical specialty. Seattle metropolitan hospital with 54,000 annual visits. Excellent salary in a stable growing group. Contact Dan Hiatt in care of Linda Johnson, 8009 S. 180th, Ste 110, Kent, WA 98032; (206) 575-2595.

OTOLARYNGOLOGIST. BC/BE to join 28 physician multispecialty group practice. Located in beautiful Pacific northwest between Seattle and Vancouver, BC. Contact Shane Spray, 1400 E. Kincaid, Mount Vernon, WA 98273.

FAMILY PRACTICE PHYSICIAN. Full-time in a busy walk-in medical clinic. Located in Visalia, California (Tulare County). Malpractice insurance, good salary, etc. Please call (209) 627-5555 for more information.

ASSOCIATE IN PEDIATRICS. Kern Medical Center, Bakersfield, California, a teaching hospital affiliated with UCLA and UCI Schools of Medicine, seeks an Associate in the Division of Pediatrics. Prerequisites include eligibility or certification by the American Board of Pediatrics, strong interest in teaching and qualifications for faculty appointment in UCLA Department of Pediatrics. Comprehensive salary and benefit package. A part-time private practice is permitted. Medical center is in central California, a mid-sized urban community with moderate cost of living. Send CV and inquiries to Navin Amin, MD, Chairman, Department of Family Practice/Pediatrics, Kern Medical Center, 1830 Flower St, Bakersfield, CA 93305.

(Continued on Page 382)

(Continued from Page 381)

PHYSICIANS WANTED

JUST SAY "NO"

. . . to long commutes, traffic jams, high crime and "YES" to an exceptional practice opportunity for you and great quality of life for your family. Dakota Clinic in Fargo, North Dakota, has exceptional practice opportunities in its North Dakota and Western Minnesota locations in the following specialties:

- CARDIOTHORACIC SURGERY
- FAMILY PRACTICE
- GENERAL SURGERY
- INTERNAL MEDICINE
- NEUROLOGY
- NON-INTERVENTIONAL CARDIOLOGY
- OB/GYN
- OPHTHALMOLOGY
- ORTHOPEDICS
- OTOLARYNGOLOGY
- PEDIATRICS
- PSYCHIATRY
- RADIATION ONCOLOGY
- RADIOLOGY

Dakota Clinic, a 152 physician multispecialty clinic with 16 satellite referral centers, prides itself in state-of-the-art facilities and communities with exceptional amenities. We offer a very competitive salary and benefit package along with a strong administrative and support staff to assist in your practice.

To receive our video and community/practice information call:

DICK REIS, RECRUITING MANAGER
DAKOTA CLINIC, LTD
1702 S UNIVERSITY DR
FARGO, ND 58103
(800) 342-4926

MARKS MEDICAL PLACEMENTS

Joyce Marks—President

Immediate opportunities for BC/BE physicians in Southern and Northern California, **Family Practice, Internal Medicine, OB/GYN.**

Please send CV to:

Marks Medical Placements
5700 Etiwanda Ave, Ste 287
Tarzana, CA 91356

Or Call:

(818) 345-1059, FAX (818) 996-6741.

AT NO COST TO PHYSICIAN

PALO ALTO MEDICAL CLINIC, a 150 physician multispecialty group with a national reputation for innovation and excellence, seeks BC Family Practice or Emergency Medicine physicians for full-time practice in Urgent Care facility. Occupational Medicine experience desirable. Competitive salary based on experience. Excellent benefits package. Two year partnership track. Please forward letter of interest and CV to George Perlstein, MD, Medical Director, Palo Alto Medical Clinic, 300 Homer Ave, Palo Alto, CA 94301.

SOUTHERN CALIFORNIA. Family Practitioner needed by 20 physician Primary Care group. Several requirements have created opportunity for future partner. Generous salary and benefit package in return for commitment to quality. Location is 45 minutes east of beaches. Contact Ken Baker, Physician Search Group, 550 Montgomery St, Ste 725, San Francisco, CA 94111; (800) 229-0411 or FAX (415) 399-0411.

PHYSICIANS WANTED

CALIFORNIA

Primary Care Physicians and Radiologists needed to work as locum tenens statewide. High salary, paid malpractice. Work whenever and wherever you wish. Permanent placements as well. **INTERIM PHYSICIANS, formerly Western Physicians Registry: Northern California, contact Jim Ellis, (800) 437-7676. Southern California, contact Tracy Zweig, (800) 635-3175.**

TWO BC/BE OB/GYNs with commitment to caring for the underserved, needed to join 13 physician (OB, Family Practice, Pediatrics, Internal Medicine), Primary Care community health clinic in Toppenish and Grandview, Washington, which has a four physician team (Family Practice, OB, Internal Medicine). Rural setting, beautiful sunny central Washington near Columbia River Gorge. Diverse cultural influences (Hispanic and Native American). Recreational opportunities including fishing, skiing, and bikers' paradise. Competitive salary with excellent benefit package including vacation up to 32 days per year and paid professional liability. Contact Ann Garza, Director of Personnel, or Jeri Weeks, Personnel Assistant, Yakima Valley Farm Workers Clinic, PO Box 190, Toppenish, WA 98948; (509) 865-5898.

NEW MEXICO. Excellent opportunity for BC/BE OB/GYN, Internal Medicine, and Family Practice to join successful practices or start new in a growing community. Plan on full practice from the beginning. Enjoy sunshine, skiing, hiking, fishing, and hunting in a southwestern lifestyle. For further information on benefits and compensation contact Anne Winter, RN, Director Prof. Development, St. Joseph Healthcare System, Albuquerque, NM; (505) 246-8003.

RICHLAND, WASHINGTON is extending an invitation to a BC Rheumatologist to practice in its community. Strong referral base. State-of-the-art hospital. Abundant recreation and quality lifestyle. Competitive income guarantee. Start up assistance and practice management consulting provided. Send CV or call Christian Rebhun, Jackson and Coker, Inc, 115 Perimeter Center Pl, Ste 380 12178, Atlanta, GA 30346; telephone (800) 544-1987.

FAMILY PRACTICE PHYSICIAN needed for hospital clinic adjacent to 32-bed hospital. Full-range practice has regular hours and one in three call. Located near Lake Sakakawea in western North Dakota. Low crime as well as abundant recreational amenities including an 18-hole golf course, great fishing, and hunting. $100,000 salary with production incentives, full benefits, and paid malpractice. This is a management-free practice. Send CV or call Christian Rebhun, Jackson and Coker, Inc, 115 Perimeter Center Pl, Ste 380 12191, Atlanta, GA 30346; telephone (800) 544-1987.

MONTEREY BAY. Midway between Santa Cruz and Monterey, this unpretentious community is perfect for the hiker, biker, surfer, and outdoorsperson. Medical staff is cohesive and anxious to welcome additional Family Physicians, Pediatricians, and General Internists. Group and independent practice with call schedules which allow time for lifestyle. Contact Ken Baker, Physician Search Group, 550 Montgomery St, Ste 725, San Francisco, CA 94111; (800) 229-0411, or FAX (415) 399-0411.

TWO INVASIVE CARDIOLOGISTS AND FAMILY PHYSICIANS NEEDED. Unique opportunity. Gorgeous California central coast. Partnership within year. Send references/CV to PO Box 220, 395 Del Monte Center, Monterey, CA 93940.

FAMILY PRACTICE/INTERNAL MEDICINE. Three Physicians wanted for two locations (Merced, Loma Linda areas). No administration. Six-figure salary plus monthly profit sharing, malpractice (including tail) paid, other fringes. Call Mike Buker, Administrator, Medical Advantage; (209) 383-3990, or send CV to 750 W Olive Ave, Ste 104, Merced, CA 95348.

(Continued on Page 383)

(Continued from Page 382)

PHYSICIANS WANTED

NATIONWIDE TRAVEL. Health research organization seeks physician for National Health and Nutrition Examination Survey sponsored by the US Public Health Service. Individual will be part of a large medical team conducting health examinations in government mobile exam centers traveling to 88 areas of the US through Fall of 1994. Must be licensed in one state. One year minimum commitment and full-time continuous travel required. Competitive salary, paid malpractice, per diem, car, four weeks paid vacation per year, holidays, and health, life, dental, disability insurance offered. Call Beverly Geline, (800) 937-8281, ext 8248. Westat, Inc, Rockville, MD, EOE/M/F/V/H.

NEVADA—GASTROENTEROLOGIST. BC/BE needed to join General Intern practice in southern Nevada. Generous salary leading to full partnership. Interest in Internal Medicine preferred. Send CV to K. Hicks, 6151 Mountain Vista, #525, Henderson, NV 89014.

DERMATOLOGY. BC/BE Dermatologist needed for busy Medical/Surgical practice. Located in wonderful recreational area on California's beautiful central coast. Ideal location for families, close to lake, ocean, university campus. Surgical and/or pathology skills preferred. Partnership potential. Send résumé to Number 268, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

PULMONARY/CRITICAL CARE. Immediate opening for BC/BE Pulmonologist to join two BC Pulmonologists/Intensivists in expanding practice located in a desirable southern California seaside community. This outstanding opportunity provides a 100% Pulmonary/Critical Care consultative practice, academic affiliations/teaching position available locally. Please reply with a letter of introduction and CV to Number 269, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

(Continued on Page 384)

California Department of Corrections

Physicians

The California Department of Corrections currently has a number of opportunities available for INFECTIOUS DISEASE PHYSICIANS (AIDS) in our Vacaville facility, as well as other locations throughout the state. In addition, openings exist for INTERNAL MEDICINE/PRIMARY CARE PHYSICIANS in the following locations:

- Susanville
- Madera
- Wasco
- Corcoran
- Blythe
- Crescent City
- Tehachapi
- Ione
- Jamestown
- San Quentin
- Calipatria
- Vacaville

Most positions are very flexible: full-time, part-time, and contract consultant positions are available (full-time preferred). Earn up to $98,000 annually PLUS State of California benefits which are excellent.

DEPUTY WARDEN, Clinical Services - Vacaville
Up to $99,828 (ask about proposed bonus)

CHIEF MEDICAL OFFICER - Chino

If you are interested in opportunities that provide professional growth, innovation, and a challenge, call

(916) 327-7081 or

Send Curriculum Vitae to: P.O. Box 161329- PPD Sacramento, CA 95816. EOE.

(Continued from Page 383)

PHYSICIANS WANTED

KAISER PERMANENTE

Good People. Good Medicine.

NORTHERN CALIFORNIA

Several positions available for Internal Medicine, most medical subspecialties, ENT, Orthopedics, Anesthesiology, and OB/GYN. We are a young, aggressive group in a well known prepaid group practice HMO organization with excellent benefits and a very reasonable call schedule. You will have a rewarding practice opportunity with ample time to enjoy the mountains and San Francisco which are nearby. If interested please call or send CV to Physician Recruitment, Administration, The Permanente Medical Group, Inc, 1305 Tommydon St, Stockton, CA 95210; (209) 476-3300.

ORTHOPEDIC SURGEONS. Orthopedic surgeon for a very busy Orthopedic service in a 223-bed teaching hospital with residencies in General Surgery, Internal Medicine, OB/GYN, and Family Practice. Should be BC/BE. Experience in arthroscopy preferred. Salary and compensation plan negotiable depending on experience. Hospital located in beautiful northern San Joaquin Valley close to major cities and skiing areas. Please submit CV and references or contact Nathaniel Matolo, MD, Chief of Surgery, San Joaquin General Hospital, PO Box 1020, Stockton, CA 95201; phone (209) 468-6600. AA/EOE.

PHYSICIANS WANTED

BC/BE FAMILY PRACTITIONER for satellite clinic of prestigious multispecialty group practice. Join one other Family Practitioner and one Physician's Assistant in small town setting with urban culture 20 minutes away. Generous benefit package. Send CV to Donald Benz, MD or Karen Stanton, The Vancouver Clinic Inc, PS, 700 NE 87th Ave, Vancouver, WA 98664; (206) 254-1240.

SEATTLE, WASHINGTON. FAMILY PHYSICIAN BC/BE, part- or full-time, wanted for a stimulating practice in a comprehensive Primary Care community clinic serving a diverse Asian/Pacific Islander population. OB required. Cantonese language skills helpful. Contact Debra Cavinta, Administrative Assistant, International District Community Health Center, 416 Maynard Ave S, Seattle, WA 98104; (206) 461-3617. EOE. Closing Date 9/30/92.

NATIONWIDE. Urgent Care, Family Practice, and Emergency Physicians are now needed in multiple locations which include Idaho, North Carolina, Virginia, Alabama, Arizona, and more. Please send your CV to Barbara Miller, Snake River Physicians, 2995 N Cole Rd, Ste 200B, Boise, ID 83704, or call Barbara Miller at (800) 688-5008.

DISCOVER IDAHO. Urgent Care, Family Practice, and Emergency Physicians are now needed for a Low Acuity AFB Emergency Department, with an annual volume of 16K, and for an Urgent Care clinic with an annual volume of 15K. Here is your chance to live and work in one of America's fastest growing and most desirable areas. This attractive location offers the convenience and amenities of a major metropolitan area—where recreation is limited only by your imagination. Benefits include flexible scheduling, with the option of 12 or 24 hour shifts, competitive salaries, and no on-call duty. For more information please call or send your CV to Barbara Miller, Snake River Physicians, 2995 N Cole Rd, Ste 200B, Boise, ID 83704; (800) 688-5008.

PHYSICIANS WANTED

NORTHERN CALIFORNIA—LOS GATOS

FAMILY PHYSICIAN needed to replace physician leaving. Full-time, Monday thru Friday. Share on-call with six other physicians. Close to Good Samaritan Hospital. Full lab and x-ray in office. For more information, contact Teri Daniels; (408) 377-9180.

GENERAL INTERNIST in the Pacific Northwest. Busy 30 physician multispecialty group practice looking for General Internist with ICU skills and interests to join existing Internal Medicine department. Competitive salary and benefits. Send CV to Shane Spray, 1400 E. Kincaid, Mount Vernon, WA 98273.

MAJESTIC SKAGIT VALLEY IN WESTERN WASHINGTON has multispecialty group seeking eighth Family Practitioner. BE/BC, OB optional. Competitive salary and benefits. If interested, send CV to Shane Spray, 1400 E. Kincaid, Mount Vernon, WA 98273.

ESCAPE those urban hassles and come to scenic northern California, southern California, and Phoenix, Arizona. Opportunity available to join two other Internists in private practice. Competitive salary and benefit package available. Contact Mark Oswald of Gielow/Laske Associates, Inc, 306 N Milwaukee St, Milwaukee, WI 53202; (800) 969-7715, FAX (414) 226-4131. Confidential inquiries welcome.

EXCELLENT OPPORTUNITY FOR INTERNAL MEDICINE PHYSICIAN in private practice multispecialty physician group in San Francisco. Income guarantee. No investment. Forward CV to Box 263, The Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

DERMATOLOGIST. Immediate opportunity available for full- or part-time position with University affiliated multispecialty group in one of the most desirable cities. We offer a balanced lifestyle, competitive salary and an excellent benefit package. Send CV to Mary Anderson, Personnel Representative, Pacific Medical Center, 1200 12th Ave S., Seattle, WA 98144; (206) 326-4111.

BC/BE FAMILY PHYSICIAN to join three other Family Practitioners, OB/GYN, Internist, and Physician Assistant at busy Migrant/Community Clinic in Grandview, Washington. Full-range Family Practice, including Obstetrics, hospital work, and Emergency coverage. Excellent relationship with well trained BC Family Practitioners and surgeon in community. Friendly rural area with good schools. Close to mountain recreational areas and water sports. Professional liability paid. Excellent benefits, vacation liberal. Contact Ann Garza, Director of Personnel, or Jeri Weeks, Personnel Assistant, Yakima Valley Farm Workers Clinic, PO Box 190, Toppenish, WA 98948; (509) 865-5898.

DON'T FORGET!

The deadline for submitting classifieds for the November issue of WJM is September 25. Send your advertisement to:

Classified Advertising
WJM, PO Box 7602
San Francisco, CA 94120-7602
(415) 882-3376

(Continued on Page 385)

(Continued from Page 384)

PHYSICIANS WANTED

UROLOGISTS—BC/BE needed for multispecialty group practice in central California and single-specialty group in Tucson, Arizona. Excellent compensation packages and partnership opportunity. All inquiries confidential. Mitchell & Associates, Inc, PO Box 1804, Scottsdale, AZ 85252; (602) 990-8080.

AMBULATORY/FAMILY PRACTICE group seeking Family Practice/General Practice physician for rapidly expanding practice in northern California. Prime recreation area in growing community of 70,000. Compensation and benefits include malpractice, health insurance, and CME. Call (916) 222-2113 or send résumé to 191 Hartnell Ave, Redding, CA 96002.

BE/BC PHYSICIANS. Moreno Valley Medical Group. General Practitioner, OB/GYN, Internal Medicine. Excellent compensation. Send CV to Moreno Valley Medical Group, 22810 Alessandro Blvd, Moreno Valley, CA 92388. Call (714) 653-2500 (Marcel).

TWO EMERGENCY OR FAMILY PRACTICE PHYSICIANS BE/BC needed to staff two clinics in Bellingham, Washington. One clinic is Primary Care; one is Ambulatory Care. No OB required. Desirable northwest location where water and mountains meet. Income guarantee. Equity opportunity. Send CV to PO Box 1644, Blaine, WA 98230.

HIV EARLY INTERVENTION PROGRAM needs full-time Primary Care or Internal Medicine physician to work within innovative outpatient setting. Opportunity to follow HIV-positive patients through full spectrum of care along with multidisciplinary staff. Teaching and hospital attending opportunities available. Salary and benefits are competitive and based upon experience. Contact Martin Fenstersheib, MD, Public Health Medical Services, 2220 Moorpark Ave, San Jose, CA 95128; (408) 299-5858.

(Continued on Page 386)

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PHYSICIANS WANTED

DEAR DOCTOR:

If your goals include a quality lifestyle, a dynamic medical community, excellent schools/universities, and beautiful and affordable housing, then we have the ideal practice opportunity for you!

HOLY FAMILY HOSPITAL and the MEDICAL STAFF are working together to meet the healthcare demands of our 150,000 patient population. There is an IMMEDIATE need for BC/BE physicians in the following specialties:

- FAMILY PRACTICE
- PEDIATRICS
- INTERNAL MEDICINE
- CARDIOLOGY
- PSYCHIATRY
- ORTHOPEDICS
- GENERAL SURGERY

SPOKANE, WASHINGTON (370K metro population) is the regional Healthcare and Cultural center offering a sound economy, unlimited outdoor recreation and a mild four season climate.

CONTACT with CV to: **Nancy Chaffins**

HOLY FAMILY HOSPITAL

N. 5633 LIDGERWOOD
SPOKANE, WA 99207
(509) 482-2164
FAX: (509) 482-2187

NORTHERN CALIFORNIA PEDIATRICS. BC/BE Pediatrician to join three Pediatricians and two Nurse Practitioners in beautiful northern California coastal city. Competitive salary first year, then partnership if mutually agreeable. Contact C. Cody, MD, 2800 Harris St, Eureka, CA 95501; (707) 445-8416.

HEMATOLOGY/ONCOLOGY. Practice in the world famous Napa Valley grape growing region, 90 minutes north of San Francisco. Strong referral base with service area of 65,000. Competitive income guarantee, coverage and privileges at esteemed 160-bed hospital. Call Anders Karlman, Karlman Associates, 1118 Pine St, Ste 124, St. Helena, CA 94574; (800) 634-3561, FAX (707) 963-2769.

PRACTICE ON KAUAI. Urgent Care/Family Medicine Practice in a 45 doctor quality oriented multispecialty group. Walk-in clinic in central facility plus coverage in various satellite clinics on the island. Subtropical climate, all ocean sports, golf, tennis, hiking year round. Night call not required, unless inpatient practice desired. Competitive salary, excellent benefits, congenial group. Preference given to candidate available soon. Send CV to Rex D. Couch, MD, Medical Director, Kauai Medical Group, Inc, 3420-B Kuhio Hwy, Lihue, HI 96766.

GILROY, CALIFORNIA. BC INTERNIST to join established but growing private practice in Gilroy, California. Ideal candidate will have one to two years practice experience. Guaranteed salary and benefits. Excellent practice opportunity in this growing community. Send CV to Number 272, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

PHYSICIANS WANTED

INTERNIST

The Motion Picture & Television Fund healthcare center in Woodland Hills has an immediate opening for a BC Internist. You will provide outpatient and acute inpatient medical care for patients within a diverse adult age range. For consideration, please forward your CV directly to ADMINISTRATION.

TV & MOTION PICTURE FUND
23388 Mulholland Dr
Woodland Hills, CA 91364
Equal Opportunity Employer

CALIFORNIA PALM SPRINGS AREA. BC/BE Emergency or Family Practice physician or experienced in Urgent Care for a growing, state-of-the-art Urgent Care clinic. Paid malpractice. Salary plus profit sharing. Contact Govind Sharma, MD, FACEP, Palm Desert Urgent Care, 73-345 Hwy 111, Palm Desert, CA 92260; (619) 340-5800.

INTERNAL MEDICINE/PRIMARY CARE. BC/BE, recently trained (university program preferred) for group practice in San Francisco. Send CV and availability to A. Aronow, MD, 45 Castro St, San Francisco, CA 94114.

SANTE FE, NEW MEXICO. Occupational Physician for expanding practice in Sante Fe, New Mexico. Must have an interest in musculoskeletal injuries, IMEs, and evaluations. Multi-physician operation with trained staff, an affiliate of a larger Occupational Medicine Group. Medical directorship a possibility. BC/BE preferred. Come to the Land of Enchantment in a multicultural setting with extensive outdoor recreational activities, including skiing, rafting, hiking, etc. Positions also available in Albuquerque. Contact Gary Dunn, Administrator; (800) 866-2467 or FAX CV to (505) 842-5676.

ONCOLOGY. Excellent opportunity for BC/BE Oncologist with an interest in clinical research. Associate with premier Oncology group in Billings, Montana. Practice offers competitive income guarantee, full benefits, and insurance. One year to partnership with excellent growth potential. Offices are adjacent to state-of-the-art, 280-bed hospital and regional cancer treatment center. Billings is a beautiful city of 100,000 offering exceptional cultural and recreational amenities. Send CV or call Chris Rebhun, Jackson and Coker, Inc, 115 Perimeter Center Pl, Ste 380 12236, Atlanta, GA 30346; telephone (800) 544-1987.

BC/BE OB/GYN AND FAMILY PRACTITIONER with commitment to caring for the underserved, needed to join one Family Nurse Practitioner, one Pediatric Nurse Practitioner, and one OB/GYN Nurse Practitioner in Walla Walla, Washington. Shared call with two local OB/GYNs and four Family Physicians. Diverse cultural influences. Rural setting, abundant recreational opportunities. Competitive salary, NHSC loan repayment slots, professional liability, excellent benefit package including vacation up to 32 days per year. Contact Ann Garza, Director of Personnel, or Jeri Weeks, Personnel Assistant, (509) 865-5898, or Sylvia Arroyo, Clinic Administrator, (509) 525-6650.

INTERNIST BC/BE to join 10 physician (OB, Pediatrics, Internal Medicine), Primary Care community health clinic in Toppenish, Washington serving migrant and seasonal farm workers with common as well as Third World maladies. Reasonable call schedule with 3.5 Internal Medicine department. Rural setting, beautiful, sunny central Washington near Columbia River Gorge. Diverse cultural influences (Hispanic and Native American). Recreational opportunities including fishing, skiing, and bikers' paradise. Competitive salary with excellent benefit package including vacation up to 32 days per year and professional liability. Contact Ann Garza, Director of Personnel, Yakima Valley Farm Workers Clinic, PO Box 190, Toppenish, WA 98948; (509) 865-5898.

PHYSICIANS WANTED

PORTLAND, OREGON. Unique opportunity for Internist to join three Internal Medicine faculty members at large urban teaching hospital, in private practice and faculty activities. Fully equipped, modern facility. If you have a clinical area of special interest, General Medicine, and teaching skills, this is an exciting opportunity to build a practice in the scenic Pacific Northwest. Excellent compensation package. Send CV to Ken Scissors, MD, PO Box 29114, Portland, OR 97209.

NON-PATIENT CARE POSITIONS in California and nationwide. Your medical training is sought after in industry. For listing information send a post card with your name, address, phone, FAX, qualifications, any foreign language skill, health status, age and description of current activity. "MD NON MD," 789 Knapp Dr, Montecito, CA 93108-1908.

PRIMARY CARE PHYSICIAN for an active practice with Clinic and Hospital responsibilities. Please send CV or résumé to Casa Grande Clinic, PC, Attn: Rick O'Neil, 1023 E Florence Blvd, Casa Grande, AZ 85222.

(Continued on Page 387)

(Continued from Page 386)

PHYSICIANS WANTED

SCENIC COLORADO front range community of 30,000, with a strong, growing economic base, needs Family Physicians. Join a group of physicians or establish a solo practice with cross coverage. Full range of Family Medicine, including OB, available. Hospital offers generous guarantee for the physician wanting to be close to Rocky Mountain recreation as well as metropolitan areas. Call Rita Longino at (800) 279-5267, or FAX CV to (800) 467-1246, or send CV to WHS, PO Box 2107, Corrales, NM 87048-2107.

NORTHERN CALIFORNIA HOSPITAL seeking a BC/BE Internist to staff its new satellite medical clinics. Assistance is available in establishing a practice. Net income guarantees are open including support for office staff and required equipment. Contact Margaret Ward, Redbud Community Hospital, PO Box 6720, Clearlake, CA 95422; (707) 994-6486, ext 128.

SAN FRANCISCO BAY AREA—FAMILY PRACTITIONER, PEDIATRICIAN, PSYCHIATRIST. Recently trained, energetic, enthusiastic, BC preferred, for 18 physician Palo Alto Medical Clinic satellite. Clinic is progressive 150 physician multispecialty group known for innovation and excellence. Practice is established and growing. Excellent location, convenient access to San Francisco and Stanford. Excellent compensation/benefits package. Please send CV and letter of interest to David Hooper, MD, Medical Director, Palo Alto Medical Foundation, 39500 Liberty St, Fremont, CA 94538.

OREGON. Immediate opportunities for Family Practitioners with or without Obstetrics to join busy practices in Oregon's Willamette Valley. Rural lifestyle with easy access to cities, beautiful area, great medical community and $5,000 Oregon State Tax Credit. Contact Beverly Day, Lebanon Community Hospital, Box 739, Lebanon, OR 97355; (503) 451-7110.

PHYSICIANS WANTED

RADIOLOGISTS

DVI Health Services Corporation, a publicly traded company on the New York Stock Exchange, has opportunities for Radiologists in outpatient diagnostic imaging facilities located in various states. Immediate openings are available in Arizona and Wisconsin for individuals with extensive MRI experience and credentials, and in Arizona for individuals with General Radiology experience. Send résumé to **Cynthia Cohn, DVI Health Services Corporation, One Park Plaza, Ste 800, Irvine, CA 92714; or call (714) 474-5800.** Compensation commensurate with experience.

LARGE MULTISPECIALTY MEDICAL GROUP needs General Internist to join our six person department. Beautiful environment for enjoyable practice. Excellent salary, benefits, and free time. Send CV to Rex Couch, MD, Medical Director, Kauai Medical Group, Inc, 3420-B Kuhio Hwy, Lihue, HI 96766.

URGENT CARE/PRIMARY CARE PHYSICIANS. Current permanent positions available in Phoenix, Denver, Colorado Springs. Attractive settings with reasonable workload. Enticing locum tenens assignments available also throughout the Rocky Mountain west. Call or write Ed Novelli, Interim Physicians, 4155 E Jewell, Ste 1018, Denver, CO 80222; (800) 669-0718.

GENERAL INTERNIST—OREGON. BC/BE General Internist to join 21 member Internal Medicine department of 62 physician multispecialty clinic. University town. Guaranteed salary, incentive bonus, excellent benefits. Send CV to Richard M. Rytting, MD, Medical Director, The Corvallis Clinic, PC, 3680 NW Samaritan Dr, Corvallis, OR 97330.

PHYSICIANS WANTED

FAMILY PRACTICE. Practice in the world famous Napa Valley grape growing region, 90 minutes north of San Francisco. Established group of three physicians has an opening due to a retirement. Competitive income guarantee, coverage and privileges at esteemed 160-bed hospital. Call Anders Karlman, Karlman Associates, 1118 Pine St, Ste 124, St. Helena, CA 94574; Telephone (800) 634-3561, FAX (707) 963-2769.

GENERAL INTERNIST. The VA Medical Center, Long Beach, California is recruiting for a Staff Physician. Duties include seeing patients in the Walk-in-Clinic, supervision, and teaching of house staff in the clinic. The VA is affiliated with the College of Medicine at the University of California, Irvine. Vacancy is full-time position, 40 hours per week. US citizenship is required. Please send CV to David Webb, MD, Associate Chief of Staff, Ambulatory Care (153). The VA is an Equal Opportunity Employer.

INTERNAL MEDICINE. Live in a thriving central valley California community (pop: 30,000 drawing: 120,000) that still offers reasonable housing prices, no traffic jams and easy access to mountains and beaches. Choose between group or solo practice. Competitive guarantees and coverage. Call Anders Karlman, Karlman Associates, 1118 Pine St, Ste 124, St. Helena, CA 94574; (800) 634-3561, FAX (707) 963-2769.

SOUTHEASTERN NEW MEXICO has a comfortable lifestyle and a need for Primary Care physicians. Clovis, New Mexico is a growing community with vital practice and lifestyle opportunities. Financial packages and practice management services are available from Clovis High Plains Hospital, an affiliate of Presbyterian Healthcare Services. Contact either Bill Norris; (800) 545-4030, ext 6320, or Grant Nelson; (800) 221-3706 for details.

(Continued on Page 388)

(Continued from Page 387)

DON'T FORGET!

The deadline for submitting classifieds for the November issue of WJM is September 25. Send your advertisement to:

Classified Advertising
WJM, PO Box 7602
San Francisco, CA 94120-7602
(415) 882-3376

SAN DIEGO COUNTY. Family, Internal, OB/GYN, and Pediatric practices available. Long established—doctors retiring. Various prices and low down payments. Call CBI, San Diego County's professional practice sales specialists, (619) 283-7009.

SANTA BARBARA COUNTY OB/GYN practice for sale. Wonderful climate. Safe family environment. Patient load priv/HMO/PPO contract. Medi-Cal clients, if so inclined. Gross $288 K. Terms for sale very appealing. Will stay to introduce. Start this summer. A rare opportunity. Number 271, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

PUGET SOUND (WITH TIME TO ENJOY IT). Occupational/Sports Medicine practice. Nine years this location. Four days per week, no night or weekend call. Net 150K plus per year. Unlimited growth potential; (206) 922-6466.

SAN DIEGO AREA. Opportunities to share office space or purchase physician practice, charts and equipment near Grossmont Hospital, a 459-bed regional medical center affiliated with the largest health care provider in San Diego County, Sharp HealthCare. Specialties include ENT, Internal Medicine, Orthopaedic Surgery, Pulmonary Medicine, and Family Practice. Send CV or contact Karen Ground, Physician Services, Grossmont Hospital, PO Box 158, La Mesa, CA 91944-0158; (619) 589-4891.

THE SAN DIEGO CONFERENCE ON RESPONDING TO CHILD MALTREATMENT, Hyatt Regency Hotel, San Diego, California, January 26-30, 1993. Five intensive days of lectures, workshops, debates, open forums, task force meetings and other special educational activities with national and international leaders in the field of Child Protection. APSAC and CAPSAC Annual Meetings, APSAC Institutes. Approved for CME credits. CENTER FOR CHILD PROTECTION, Children's Hospital; for registration information please contact Robbie Webb at (619) 495-4940.

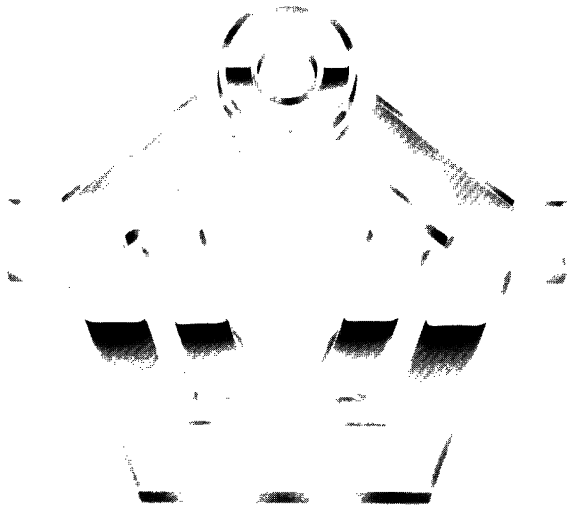
NURSE PRACTITIONERS AND PHYSICIAN ASSISTANTS. Western Practitioner Resources is California's leading placement service for mid-level practitioners. We'll find the right practitioner for your clinical setting. Please contact Heidi Bourne, RN, Director; (800) 345-5859.

MEDICAL DEVICES and procedures a specialty. Consult a registered patent attorney before you publish or practice your invention. Acronational Patent Law Firm, 101 California St, Ste 980, San Francisco, CA 94111; (415) 421-1546.

SAN FRANCISCO—Stonestown Medical-Dental Building. Established facility with good referrals. Adjacent to Stonestown Galleria at 19th Avenue. Excellent public transportation and free parking. Call (415) 564-8848.

OFFICE SPACE TO SHARE. Ophthalmology. 20 minutes east of Los Angeles. State-of-the-art. Modern. Sublet as separate practice. Flexible, any arrangement considered. Number 270, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

BRAND NEW, modern medical office building in Anaheim, fully equipped including x-ray. Excellent for Primary Care or specialist. Full- or part-time. Call (714) 772-0721.



One Of A Kind

Zantac®

ranitidine HCl/Glaxo 150 mg and 300 mg tablets

Zantac® 150 Tablets
(ranitidine hydrochloride)
Zantac® 300 Tablets
(ranitidine hydrochloride)
Zantac® Syrup
(ranitidine hydrochloride)

BRIEF SUMMARY

The following is a brief summary only. Before prescribing, see complete prescribing information in Zantac® product labeling.

INDICATIONS AND USAGE: Zantac® is indicated in:
1. Short-term treatment of **active duodenal ulcer.** Most patients heal within 4 weeks.
2. **Maintenance therapy** for duodenal ulcer patients at reduced dosage after healing of acute ulcers.
3. The treatment of **pathological hypersecretory conditions** (e.g., Zollinger-Ellison syndrome and systemic mastocytosis).
4. Short-term treatment of **active, benign gastric ulcer.** Most patients heal within 6 weeks and the usefulness of further treatment has not been demonstrated.
5. Treatment of **gastroesophageal reflux disease (GERD).** Symptomatic relief commonly occurs within 1 or 2 weeks after starting therapy with Zantac 150 mg b.i.d.
6. Treatment of endoscopically diagnosed **erosive esophagitis.** Healing of endoscopically diagnosed erosive esophagitis occurs at 4 weeks (47%), 8 weeks (71%), and 12 weeks (84%) of therapy with Zantac 150 mg q.i.d. Symptomatic relief of heartburn commonly occurs within 24 hours of therapy initiation with Zantac.

Concomitant antacids should be given as needed for pain relief to patients with active duodenal ulcer; active, benign gastric ulcer; hypersecretory states; GERD; and erosive esophagitis.

CONTRAINDICATIONS: Zantac® is contraindicated for patients known to have hypersensitivity to the drug.

PRECAUTIONS: General: 1. Symptomatic response to Zantac® therapy does not preclude the presence of gastric malignancy.
2. Since Zantac is excreted primarily by the kidney, dosage should be adjusted in patients with impaired renal function (see DOSAGE AND ADMINISTRATION). Caution should be observed in patients with hepatic dysfunction since Zantac is metabolized in the liver.
Laboratory Tests: False-positive tests for urine protein with Multistix® may occur during Zantac therapy, and therefore testing with sulfosalicylic acid is recommended.
Drug Interactions: Although Zantac has been reported to bind weakly to cytochrome P-450 *in vitro*, recommended doses of the drug do not inhibit the action of the cytochrome P-450-linked oxygenase enzymes in the liver. However, there have been isolated reports of drug interactions that suggest that Zantac may affect the bioavailability of certain drugs by some mechanism as yet unidentified (e.g., a pH-dependent effect on absorption or a change in volume of distribution).

Increased or decreased prothrombin times have been reported during concurrent use of ranitidine and warfarin. However, in human pharmacokinetic studies with dosages of ranitidine up to 400 mg per day, no interaction occurred; ranitidine had no effect on warfarin clearance or prothrombin time. The possibility of an interaction with warfarin at dosages of ranitidine higher than 400 mg per day has not been investigated.
Carcinogenesis, Mutagenesis, Impairment of Fertility: There was no indication of tumorigenic or carcinogenic effects in life-span studies in mice and rats at dosages up to 2,000 mg/kg per day.

Ranitidine was not mutagenic in standard bacterial tests (*Salmonella, Escherichia coli*) for mutagenicity at concentrations up to the maximum recommended for these assays.

In a dominant lethal assay, a single oral dose of 1,000 mg/kg to male rats was without effect on the outcome of two matings per week for the next 9 weeks.
Pregnancy: ***Teratogenic Effects: Pregnancy Category B:*** Reproduction studies have been performed in rats and rabbits at doses up to 160 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to Zantac. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.
Nursing Mothers: Zantac is secreted in human milk. Caution should be exercised when Zantac is administered to a nursing mother.
Pediatric Use: Safety and effectiveness in children have not been established.
Use in Elderly Patients: Ulcer healing rates in elderly patients (65-82 years of age) were no different from those in younger age-groups. The incidence rates for adverse events and laboratory abnormalities were also not different from those seen in other age-groups.

ADVERSE REACTIONS: The following have been reported as events in clinical trials or in the routine management of patients treated with Zantac®. The relationship to Zantac therapy has been unclear in many cases. Headache, sometimes severe, seems to be related to Zantac administration.
Central Nervous System: Rarely, malaise, dizziness, somnolence, insomnia, and vertigo. Rare cases of reversible mental confusion, agitation, depression, and hallucinations have been reported, predominantly in severely ill elderly patients. Rare cases of reversible blurred vision suggestive of a change in accommodation have been reported. Rare reports of reversible involuntary motor disturbances have been received.
Cardiovascular: As with other H_2-blockers, rare reports of arrhythmias such as tachycardia, bradycardia, atrioventricular block, and premature ventricular beats.
Gastrointestinal: Constipation, diarrhea, nausea/vomiting, abdominal discomfort/pain, and rare reports of pancreatitis.
Hepatic: In normal volunteers, SGPT values were increased to at least twice the pretreatment levels in 6 of 12 subjects receiving 100 mg q.i.d. intravenously for 7 days, and in 4 of 24 subjects receiving 50 mg q.i.d. intravenously for 5 days. There have been occasional reports of hepatitis, hepatocellular or hepatocanalicular or mixed, with or without jaundice. In such circumstances, ranitidine should be immediately discontinued. These events are usually reversible, but in exceedingly rare circumstances death has occurred.

Zantac®150 and 300 (ranitidine hydrochloride) Tablets
Zantac® (ranitidine hydrochloride) Syrup

Musculoskeletal: Rare reports of arthralgias.
Hematologic: Blood count changes (leukopenia, granulocytopenia, and thrombocytopenia) have occurred in a few patients. These were usually reversible. Rare cases of agranulocytosis, pancytopenia, sometimes with marrow hypoplasia, and aplastic anemia and exceedingly rare cases of acquired immune hemolytic anemia have been reported.
Endocrine: Controlled studies in animals and man have shown no stimulation of any pituitary hormone by Zantac and no antiandrogenic activity, and cimetidine-induced gynecomastia and impotence in hypersecretory patients have resolved when Zantac has been substituted. However, occasional cases of gynecomastia, impotence, and loss of libido have been reported in male patients receiving Zantac, but the incidence did not differ from that in the general population.
Integumentary: Rash, including rare cases suggestive of mild erythema multiforme, and, rarely, alopecia.
Other: Rare cases of hypersensitivity reactions (e.g., bronchospasm, fever, rash, eosinophilia), anaphylaxis, angioneurotic edema, and small increases in serum creatinine.

OVERDOSAGE: Information concerning possible overdosage and its treatment appears in the full prescribing information.

DOSAGE AND ADMINISTRATION: (See complete prescribing information in Zantac® product labeling.)
Active Duodenal Ulcer: The current recommended adult oral dosage is 150 mg or 10 mL (2 teaspoonfuls equivalent to 150 mg of ranitidine) twice daily. An alternative dosage of 300 mg or 20 mL (4 teaspoonfuls equivalent to 300 mg of ranitidine) once daily at bedtime can be used for patients in whom dosing convenience is important. The advantages of one treatment regimen compared to the other in a particular patient population have yet to be demonstrated.
Maintenance Therapy: The current recommended adult oral dosage is 150 mg or 10 mL (2 teaspoonfuls equivalent to 150 mg of ranitidine) at bedtime.
Pathological Hypersecretory Conditions (such as Zollinger-Ellison syndrome): The current recommended adult oral dosage is 150 mg or 10 mL (2 teaspoonfuls equivalent to 150 mg of ranitidine) twice a day. In some patients it may be necessary to administer Zantac® 150-mg doses more frequently. Dosages should be adjusted to individual patient needs, and should continue as long as clinically indicated. Dosages up to 6 g per day have been employed in patients with severe disease.
Benign Gastric Ulcer: The current recommended adult oral dosage is 150 mg or 10 mL (2 teaspoonfuls equivalent to 150 mg of ranitidine) twice a day.
GERD: The current recommended adult oral dosage is 150 mg or 10 mL (2 teaspoonfuls equivalent to 150 mg of ranitidine) twice a day.
Erosive Esophagitis: The current recommended adult oral dosage is 150 mg or 10 mL (2 teaspoonfuls equivalent to 150 mg of ranitidine) four times a day.
Dosage Adjustment for Patients With Impaired Renal Function: On the basis of experience with a group of subjects with severely impaired renal function treated with Zantac, the recommended dosage in patients with a creatinine clearance less than 50 mL per minute is 150 mg or 10 mL (2 teaspoonfuls equivalent to 150 mg of ranitidine) every 24 hours. Should the patient's condition require, the frequency of dosing may be increased to every 12 hours or even further with caution. Hemodialysis reduces the level of circulating ranitidine. Ideally, the dosing schedule should be adjusted so that the timing of a scheduled dose coincides with the end of hemodialysis.

HOW SUPPLIED: Zantac® 150 Tablets (ranitidine HCl equivalent to 150 mg of ranitidine) are peach, film-coated, five-sided tablets embossed with "ZANTAC 150" on one side and "Glaxo" on the other. They are available in bottles of 60 (NDC 0173-0344-42) and 100 (NDC 0173-0344-09) tablets and unit dose packs of 100 (NDC 0173-0344-47) tablets.

Zantac® 300 Tablets (ranitidine HCl equivalent to 300 mg of ranitidine) are yellow, film-coated, capsule-shaped tablets embossed with "ZANTAC 300" on one side and "Glaxo" on the other. They are available in bottles of 30 (NDC 0173-0393-40) tablets and unit dose packs of 100 (NDC 0173-0393-47) tablets.

Store between 15° and 30°C (59° and 86°F) in a dry place. Protect from light. Replace cap securely after each opening.

Zantac® Syrup, a clear, peppermint-flavored liquid, contains 16.8 mg of ranitidine HCl equivalent to 15 mg of ranitidine per 1 mL in bottles of 16 fluid ounces (one pint) (NDC 0173-0383-54).

Store between 4° and 25°C (39° and 77°F). Dispense in tight, light-resistant containers as defined in the USP/NF.

May 1992
2130A

Glaxo Pharmaceuticals
DIVISION OF GLAXO INC.

Zantac® 150 Tablets/Zantac® 300 Tablets:
Glaxo Pharmaceuticals, Research Triangle Park, NC 27709

Zantac® Syrup:
Manufactured for Glaxo Pharmaceuticals, Research Triangle Park, NC 27709
by Roxane Laboratories, Inc., Columbus, OH 43216